SERIES 3, Vol. 23, No. 12 DECEMBER, 1940

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DEC 30 1940

AMERICAN JOURNAL OF OPHTHALMOLOGY

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Subscription price in United States ten dollars yearly. In Canada and foreign countries twelve Dollars. Published monthly by the George Banta Publishing Company, 450 Ahnaip Street, Menasha, Wisconsin, for the Ophthalmic Publishing Company. Subscription and Editorial Office: 640 S. Kingshighway, Saint Louis, Missouri. Entered as second class matter at the post office at Menasha, Wisconsin.

'TWAS THE DAY AFTER CHRISTMAS

'Twas the day after Christmas, and up at the Pole
St. Nick had returned from his gift giving role.
With spirits so merry and heart that was light
He thought of the presents he'd spread through the night.

"These doctors are clever," he chuckled with pride
As he counted the offices he'd been inside.
Why, during the wee hours he'd had to troop
To many a suite with a lens set or loupe.

At professional offices he'd left behind
Refractors, projectors, and things of that kind
As gifts the refractionists knew they would need
In helping their practices thrive and succeed.

"The man who invests in his practice is wise,"
He said with a gleam in his knowing old eyes,
"I've been around and I surely can tell
That he's twice as wise who buys B & L."

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EFFECT OF LOCAL INSTILLATIONS OF DRUGS ON THE PASSAGE OF FLUORESCEIN FROM THE BLOOD INTO THE ANTERIOR CHAMBER.

FIG. 1 (SWAN AND HART). MECHOLYL. CLOUD OF FLUORESCENCE IN THE AQUEOUS AT THE NASAL BORDER OF THE PUPIL (SLITLAMP BEAM).

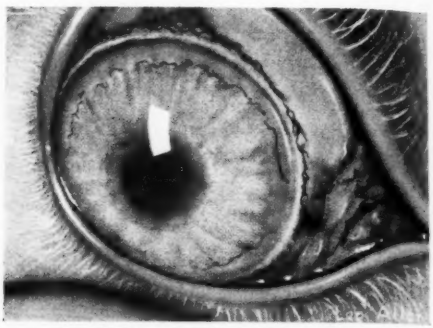

FIG. 2 (SWAN AND HART). DORYL. DISCOLORATION OF IRIS STROMA PRECEDING APPEARANCE OF FLUORESCENCE IN THE AQUEOUS (DIFFUSE LIGHT).

FIG. 3 (SWAN AND HART). DORYL. FLUORESCENCE IN THE AQUEOUS APPEARING SIMULTANEOUSLY IN THE CHAMBER ANGLE AND PUPILLARY AREA (SLITLAMP BEAM).

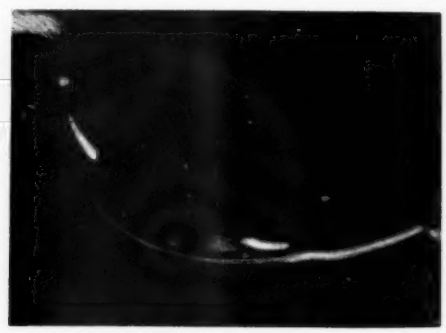

FIG. 4 (SWAN AND HART). EPINEPHRINE BITARTRATE (SECONDARY PHASE). CLOUD AT THE NASAL BORDER OF THE PUPIL (SLITLAMP BEAM).

AMERICAN JOURNAL OF OPHTHALMOLOGY

VOLUME 23 DECEMBER, 1940 NUMBER 12

A COMPARATIVE STUDY OF THE EFFECTS OF MECHOLYL, DORYL, ESERINE, PILOCARPINE, ATROPINE, AND EPINEPHRINE ON THE BLOOD-AQUEOUS BARRIER*

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Iowa City, Iowa

The blood-aqueous barrier plays an important role in the maintenance of normal ocular metabolism, and there is evidence that alterations in this barrier contribute to the pathological physiology of such diseases as glaucoma and iridocyclitis. These diseases are treated with autonomic drugs which traditionally have been classified according to action on the muscles of the ciliary body and iris. The present investigation was undertaken to ascertain the effects of autonomic drugs on the blood-aqueous barrier and to correlate these effects with changes in size of the pupil. Experimental studies were made with atropine, eserine, pilocarpine, epinephrine bitartrate, and two relatively new drugs used in the treatment of glaucoma; namely, mecholyl and doryl.

Previous studies have been reported on the effect of drugs on the blood-aqueous barrier. The efficacy of atropine in uveal infections has been attributed by Duke-Elder[1] to an increase in permeability of this barrier, but Adler[2] has offered experimental evidence suggesting a decrease in permeability as the mode of action of this drug. Adler and Landis[3] found that pilocarpine has no significant effect on the protein content of the aqueous, while Krause, Yudkin *et al.*[4] found that this drug increases the permeability of the blood-aqueous barrier to proteins and arsenicals. Several investigators have concluded that eserine increases the permeability of the barrier, but investigations on the effects of mecholyl and epinephrine bitartrate have been limited and lack confirmation. The effect of doryl on the blood-aqueous barrier has not been investigated.

As yet no standardization of criteria for the determination of the effect of drugs on the blood-aqueous barrier exists. In previous studies, emphasis has been placed on increased protein concentration in the aqueous as an indication of increased permeability. Normal constituents other than proteins have received less attention, although the concentration of the nonprotein solutes in the aqueous is less than it is in the plasma and might be expected to increase with increased permeability of the blood-aqueous barrier. However, an increase in solid constituents in the aqueous is not necessarily associated with increased permeability of the barrier. The concentration of these substances in the aqueous may be altered by variations in ocular water balance. Keys[5] found that water passes through the capillary walls more readily than do any of the serum solutes and con-

* From the Department of Ophthalmology, College of Medicine, State University of Iowa. Presented before the Association for Research in Ophthalmology, New York, June 11, 1940.

Mecholyl and doryl for this study were supplied by Merck and Company, Inc.

cluded that when functional or experimental states alter the osmotic balance between blood and tissue, readjustment tends to take place by a shift of water, and only secondarily by a shift of solutes. This mechanism must be considered in the eye as a possible factor that may modify the concentration of aqueous solutes independently of changes in the permeability of the blood-aqueous barrier. Altered metabolism of the intraocular tissues may likewise alter the concentration of aqueous solutes. Therefore, a foreign test substance that does not enter the anterior chamber when injected into the blood stream is essential to determine whether an increase in the normal constituents following the instillation of drugs is actually associated with increased permeability of the blood-aqueous barrier.

Consideration of the factors affecting the passage of molecules across the blood-aqueous barrier is essential to the selection of the test substance. Ideally, the only factor involved in permeability studies is that of relationship of the "pore-size" of the barrier to the size of the test molecule. Factors which must be controlled in permeability experiments on the blood-aqueous barrier include three "driving" forces: hydrostatic pressure, osmotic pressure, and differences in electric potential. Each of these forces has been shown to affect the fluid balance of the eye, although their roles in normal aqueous formation are unknown.

Increased hydrostatic pressure in the ocular vessels, particularly in veins and capillaries, has been demonstrated to affect the intraocular pressure. It is desirable therefore to use a test molecule that can be injected in a small volume of fluid and has no pharmacologic nor toxic effect on the vascular system.

The intraocular fluid balance is affected by abnormal alterations in the osmotic pressure of the blood. Such alterations have led to the treatment of glaucoma with intravenous injection of hypertonic solutions. The test molecule used in permeability studies must be sufficiently large to have no osmotic-pressure effects in the concentrations suitable for microanalysis.

Friedenwald and Steihler[6] have demonstrated the presence of an electric potential between the stroma and epithelium of the ciliary body which affects the direction of passage of ions to and fro through these structures. Cations and water were found to pass from the stroma to the epithelium and anions in the opposite direction. The test substance must be selected from those nonionizable organic molecules which are soluble in tissue fluids. Ions and colloids because of their electrical charges must be excluded.

The test substance should be chemically inert in tissue fluids and nontoxic so that it neither alters nor is altered by tissue metabolism. In addition, the molecule should be slightly larger than the threshold size for entrance into the anterior chamber so that simple diffusion and increased water exchange, such as might accompany an increase in blood volume, cannot be factors.

Purified dahlia inulin was found to meet the above requirements. It is a polysaccharide composed of a chain of fructose molecules. The molecular weight of inulin as determined by the thermo-electric vapor-pressure method[7] is 5,100 but due to its elongated shape, its diffusion coefficient[8] is that of a much larger molecule (15,360). Inulin passes through artificial membranes[9] (collodion and cellophane) which do not allow the passage of proteins and therefore should be a more sensitive index of increased permeability than the plasma proteins. Purified dahlia inulin is not toxic and is inert in the tissue fluids. Like all molecules of low lip-

oid solubility, its penetration into living cells is limited.[10] It is the largest molecule yet found to filter completely through the glomerular membrane, and therefore has been used extensively in renal studies.[11] However, ocular studies with such a substance have not been reported previously.

Finally, it is desirable to use other test substances whose site and time of appearance into the anterior chamber may be observed directly. This is not possible with substances such as inulin. The entrance of certain fluorescent crystalloid dyes may be detected readily with the slitlamp and corneal microscope, and may be recorded by photographic methods. Errors associated with withdrawal of aqueous and microanalysis are avoided. However, factors other than permeability of the blood-aqueous barrier affect the entrance of these dyes into the anterior chamber. The latent period required for the passage of such diffusible dyes from the blood into the aqueous may be shortened by an increased volume of blood flow independently of increased permeability of the barrier. In addition, passage of these dyes through the ciliary stroma and epithelium has been shown to be dependent on their electrical charge.[6] This factor may be limited by the use of acid, basic, and neutral dyes. Toxic damage to the endothelial walls of the capillaries has been shown to be an additional factor to be considered in studies of permeability with dyes. However, studies with dyes provide evidence confirmatory to the inulin studies and may indicate the site of action of drugs on the barrier.

Sodium fluorescein is a suitable acid dye which has had extensive use in ocular experiments. The number of neutral and basic dyes that are fluorescent and relatively nontoxic is limited. None of these was entirely satisfactory, but Rhodamine B was best. This dye was reported by Friedenwald and Stiehler[6] to be a neutral and to contain no chloride, but the dye* used in our studies was found by conductivity experiments to dissociate slightly, and the presence of chloride ions was demonstrated by precipitation methods; therefore the dye contained both neutral and basic components.

Experimental

Single instillations of atropine sulfate (2 percent), eserine salicylate (1 percent), pilocarpine nitrate (2 to 4 percent), epinephrine bitartrate (2 percent), mecholyl (10 percent), and doryl (0.75 to 1.50 percent) were made on the corneae of adult albino rabbits and the effects on the blood-aqueous barrier were studied. The concentrations selected were those in ordinary clinical use. An amount of each solution just sufficient to cover the cornea was instilled, and the cornea was exposed for several minutes after administration to avoid spread to the conjunctiva by lid action; also, by this method, systemic reactions such as alterations in blood pressure were minimized.

Mecholyl and, to a lesser extent, doryl were found to become absorbed poorly through the corneal epithelium, but upon gentle massage with the pipette tip absorption was prompt. This procedure was followed with all drugs.

In each experiment, one eye of the animal was used to determine the effect of the drug and the other was used as a control. In addition, control analyses were made on animals not receiving drugs. An effort was made to determine the effects of physiological variations in the size of the pupil on the blood-aqueous barrier, using an illumination of 100 foot-candles for constriction and total darkness for dilatation.

Aqueous was withdrawn and an analy-

* Obtained for the National Aniline and Chemical Company, Inc. Lot No. 8777.

sis made of total solids and proteins 50 to 70 minutes after instillation of the drug or onset of treatment with light or dark. Under local anesthesia (0.5-percent pontocaine), a limbic puncture was made with an extremely sharp 27-gauge needle. Without damage to the iris and without undue suction 0.25 to 0.35 c.c. of aqueous could be withdrawn. Carefully measured quantities of single (0.2 c.c.) and pooled (0.5 to 1.0 c.c.) specimens of aqueous were dried at 110°C. for 24 hours and, after cooling in a desiccator, the total solids were weighed. The precipitate was washed with several volumes of warm 70-percent ethyl alcohol to remove water-soluble components and again dried, and the protein fraction weighed. The results are shown in table 1.

TABLE 1

EFFECTS OF DRUGS ON THE PROTEIN AND NONPROTEIN SOLIDS OF THE AQUEOUS

Treatment	Number of Eyes	Average Total Solids in Aqueous in %	Range of Total Solids in %	Average Proteins in Aqueous in %	Range of Aqueous Proteins in %
Controls	119	1.075	0.975–1.15	.05–*	trace–.05
Eserine (1%)	10	1.41	1.20 –1.65	.20	.05–.30
Mecholyl (10%)	20	1.40	1.20 –1.575	.23	.06–.33
Doryl (0.75–1.5%)	17	1.295	1.15 –1.55	.08	.05–.15
Epinephrine (2%)					
(Primary phase)	10	1.075	1.05 –1.1	.05–*	trace–.06
(Secondary phase)	10	1.275	1.20 –1.4	.09	.05–.21
Pilocarpine (4%)	18	1.16	1.10 –1.25	.065	.02–.15
Light	10	1.082	0.98 –1.14	.05–*	trace–.05
Dark	10	1.075	1.10 –1.12	.05–*	trace–.05
Atropine (2%)	8	0.96	0.90 –1.05	.05–*	trace–.05

* Less than .05 percent.

Eserine, mecholyl, and doryl increased the nonprotein solids almost equally, but only eserine and mecholyl increased the protein content significantly.

The effects of epinephrine bitartrate (2 percent) on the total solids and proteins were found to fall into two phases. It has long been known that the vasoconstriction produced by local application of strong solutions of epinephrine to the conjunctiva may be followed by secondary vasodilation; this has prompted surgeons to avoid the use of strong solutions as hemostatics because of the danger of delayed hemorrhage. During the course of these experiments, repeated observations of the iris were made with the slit-lamp and corneal microscope. Dilatation of the iris vessels developed 1½ to 2½ hours after administration of the drug, although the size of the pupil remained unchanged. In one series of animals, aqueous was withdrawn for analysis one hour after administration of the drug, and in a second series 2½ hours following administration. During the primary phase no changes were noted, but in the secondary phase the total solids were definitely increased, although to a lesser extent than in the case of mecholyl or eserine.

With pilocarpine nitrate, which even in 4-percent solution was a weak miotic in rabbits, there was a slight increase in both protein and nonprotein solids.

The results with physiological variations in the size of the pupil did not vary from the controls.

Atropine produced a slight decrease in the total solids of the aqueous.

Inulin studies were also made on albino rabbits, and the drugs were administered in an identical manner, using one eye for

TABLE 2

EFFECT OF DRUGS ON THE PASSAGE OF INULIN FROM THE BLOOD INTO THE AQUEOUS

Treatment	Number of Eyes	Average Blood Inulin in mg. %	Range of Blood Inulin in mg. %	Average Aqueous Inulin in mg. %	Range of Aqueous Inulin in mg. %
Controls	128	69.4	19.5–178.6	faint trace	faint trace
Atropine (2%)	12	66.47	27.8–111.1	faint trace	0–14
Light	10	68.3	42.1– 18.3	faint trace	0–trace
Dark	10	81.4	38.4–122.4	faint trace	0–trace
Pilocarpine 2%	8	75.2	31.0–178.6	faint trace	0–10
Pilocarpine 4%	7	51.6	36.9– 91.4	faint trace	0–11
Epinephrine (2%) (Primary phase)	10	61.43	22.7–133.3	faint trace	0–10
Doryl (0.75–1.5%)	12	77.99	37.1–125.	12.	trace–16.1
Epinephrine (2%) (Secondary phase)	10	63.1	32.4– 97.5	32.5	trace– 83.5
Mecholyl (10%)	12	71.65	19.5–142.8	32.13	14.0– 63.4
Eserine (1%)	12	61.14	37.1– 98.5	35.05	18.2–108.7

the experiment and the other as a control. Twenty minutes after instillation of the drug, inulin was injected intravenously in 0.89-percent saline, in doses calculated to produce a blood-inulin concentration of 50 to 75 mg. percent. One hour after administration of the inulin, venous blood (jugular vein) and aqueous humor were withdrawn for analysis. The inulin in these fluids was hydrolized with hydrochloric acid and heat, and analyzed as fructose by modifications* of the method of Roe.[12] This is a colorimetric method dependent on the reaction of fructose with resorcinol (Selivanoff's reaction). The micromodification for aqueous analysis was found to be accurate quantitatively with concentrations of 10 mg. percent or more. Concentrations of less than 5 mg. percent were recorded as faint traces, and those of 5 to 10 mg. percent as traces. The results are shown in table 2.

Inulin was absent or present only in faint traces in the aqueous of control eyes, and in that of eyes treated with

* TECHNIQUE OF INULIN ANALYSIS

Reagents. The reagents were prepared according to the methods of Roe.[12]

Procedure for blood. One part of blood (usually 3 to 5 c.c.) was hemolyzed by the addition of 7 parts of distilled water. The proteins were precipitated by the addition of 1 part each of 10-percent zinc sulfate and 0.5 N NaOH, and removed by filtration. A 2-c.c. portion of the filtrate was placed in a test tube and 2 c.c. of 0.1-percent alcoholic solution of resorcinol and 6 c.c. of 30-percent HCl were added and mixed by shaking. The tube was placed for 10 minutes in a water bath maintained at a temperature of 75°C. A red color developed during this period. After the tube was cooled in running water, colorimetric comparisons were made with standard fructose solutions (0.1, 0.05, and 0.025 mg. per c.c.) treated in the same manner. The results were calculated in mg. of fructose per 100 c.c. of blood.

Procedure for aqueous humor. To exactly 0.2 c.c. of aqueous in a small tube were added 1.4 c.c. of distilled water, and 0.2 c.c. each of 10-percent zinc sulfate and 0.5 N NaOH. The tip of the tube was stroked gently to produce mixing. After the tube was centrifuged at about 1,500 r.p.m. for 5 minutes, 1 c.c. of the clear supernatant fluid was drawn off and placed in another small tube. In each of two similar tubes was placed 2 c.c. of standard fructose solution containing, respectively, 0.05 and 0.025 mg. per c.c. A third standard was prepared by using 1 c.c. of the 0.025-mg.-per-c.c. solution plus 1 c.c. of distilled water. To each of the four tubes, 1 c.c. of water, 2 c.c. of 0.1-percent alcoholic resorcinol, and 6 c.c. of 30-percent HCl were added. The solutions were mixed thoroughly and placed for 5 minutes in the water bath maintained at 75°C. The tubes were cooled in running water and compared in a colorimeter. The results were determined as milligrams of fructose per 100 c.c. of aqueous.

light, darkness, atropine, or pilocarpine. In those treated with doryl, small amounts of inulin were present in the aqueous of most animals. Instillations of eserine and mecholyl consistently produced an increase in the inulin content of the aqueous. With epinephrine the results of inulin studies were similar to those of the proteins and total solids; during the primary phase, inulin did not enter the aqueous, but during the secondary phase, the blood-aqueous barrier was permeable to a greater or lesser extent, the average inulin content in the 12 animals being equivalent to that with mecholyl and eserine.

Finally, to rule out the factor of slow diffusion of inulin into the eye, the blood-inulin level of two rabbits was maintained at 50 to 125 mg. percent for 48 hours. Aqueous was withdrawn at the end of that period but only faint traces of inulin were found.

Similar studies of the drugs were made with dyes whose entrance into the anterior chamber could be observed with the slitlamp and corneal microscope. Sodium fluorescein [0.75 c.c. of a 5.5-percent (isotonic) solution per pound of body weight] was injected intravenously 20 minutes after the instillation of the drug. Normally this dye produces a green discoloration of the pupillary region of the iris within 2 to 4 minutes. After 10 to 12 minutes, a faint cloud of green fluorescence appears in the aqueous at the nasal side of the pupil and gradually fills the pupillary area before spreading slowly throughout the anterior chamber.

Following eserine (20 animals) and mecholyl (20 animals) instillations, the dye appeared as a cloud in the pupillary area 4 to 8 minutes before it appeared in the control eye and the fluorescence was much more intense (fig. 1, see frontispiece).

With doryl (20 animals), the latent period required for the dye to appear in the aqueous was consistently shortened, and was usually preceded by a definite staining of the ciliary margin of the iris (fig. 2). Fluorescence appeared in the angle of the anterior chamber and in the pupillary area simultaneously (fig. 3). In seven animals, the dye appeared in the periphery of the chamber in a concentration equally great as that in the pupillary area.

With pilocarpine (2 to 4 percent), the results varied. Entrance of fluorescein into the aqueous of the treated eye preceded that into the control eye by 2 to 5 minutes in 10 of 30 animals, while in 6 animals entrance of the dye into the treated eye was delayed from 1 to 3 minutes. In 14 animals, there was no difference between the two eyes.

After atropine instillation (20 animals), the dye usually appeared in the aqueous sooner than in the control eye, but the difference in time was considered to be within the range of experimental error.

With epinephrine, the results again fell into two phases. During the primary phase, the time required for entrance of the dye into the aqueous did not vary from normal (20 animals). In the secondary phase, fluorescence in the aqueous of the treated eye preceded that in the control eye in 18 out of 20 animals. In 4 of these animals, the difference in time was less than 2 minutes, while in the remaining 14 it was 4 to 8 minutes. In the latter group the dye appeared as an intense cloud at the nasal border of the pupil (fig. 4).

Physiological variations in pupillary size did not affect the time of appearance of the dye in the anterior chamber.

The experiments were repeated with intravenous injections of Rhodamine B.

The toxicity of this dye necessitated the use of small amounts, thus lessening the concentration in the aqueous and increasing the difficulty of accurate determinations. Purplish staining of the skin, conjunctiva, and iris stroma followed the injection of 1 c.c. per pound of body weight of a saturated solution in isotonic saline. With the biomicroscope, the dye could be detected in the aqueous as a golden-yellow fluorescence. The results paralleled those with sodium fluorescein but were less conclusive. Instillation of mecholyl, doryl, eserine, or epinephrine (secondary phase) consistently resulted in a decrease in the latent period required before the dye appeared in the anterior chamber. Pilocarpine also decreased the latent period (2 to 4 minutes), in 6 of 10 rabbits. Atropine and epinephrine (primary phase) had no detectable effect.

Discussion

The inert inulin molecule is too large to pass the normal blood-aqueous barrier in albino rabbits It is probable that the entrance of inulin into the rabbit eye after administration of the drugs under discussion—that is, mecholyl, doryl, eserine and epinephrine (secondary phase) —is dependent on a mechanical decrease in the barrier between the blood and the aqueous. Such a decrease in the barrier would be expected to result in an increase in solid constituents of the aqueous, and a decrease in the latent period required for crystalloid dyes to pass from the blood into the aqueous regardless of the electrical charge. With each of the four drugs with which inulin entered the anterior chamber, a decrease in the barrier was confirmed by an increase in solid constituents of the aqueous and a decreased latent period for the passage of crystalloid dyes.

Mecholyl, doryl, eserine, epinephrine (secondary phase), and pilocarpine by local instillation have the common property of increasing the total solids of the aqueous in rabbits. Although a direct correlation cannot be made, it is interesting to note that the only other common property described for all of these drugs is the lowering of intraocular tension in glaucoma.

The effects of epinephrine bitartrate (2 percent) on the blood-aqueous barrier fall into two phases; this is in accordance with recorded observations on the effects of epinephrine salts on the peripheral blood vessels. Duke-Elder[13] has discussed these investigations although he has not described two distinct phases. He considered the possibility of the effects of epinephrine on the ocular vessels to consist of two components: contraction of the arterioles, and dilatation and increased permeability of the capillaries. Evans,[14] in discussing the effect of epinephrine on the uveal circulation, stated that its value in reducing engorgement is largely offset by a secondary congestion.

During the course of the experiments, it was noted that 2- to 4-percent pilocarpine nitrate was a weak miotic in the albino rabbit. It is entirely possible that the other ocular effects might likewise be limited and that these results do not indicate the full effects of the drug. This factor may explain the inconsistencies in the studies with dyes. However, the increase in total solids with pilocarpine was consistent, averaging approximately 8 percent above normal. The effect of pilocarpine on the protein content of the aqueous was less consistent, and although it was usually increased slightly, conclusions cannot be drawn. It is noteworthy that Adler and Landis,[3] working with cats, found that pilocarpine had no effect on the protein content of

the aqueous, while Krause, Yudkin, *et al*,[4] working with dogs, found a considerable increase. A species difference is suggested.

Studies with sodium fluorescein indicate that doryl may have an effect on the iris vessels which differs from other miotics. The staining of the peripheral iris stroma and the appearance of the dye near the chamber angle as well as in the pupillary area was observed in each of the 20 animals; this did not occur with any other miotic.

Atropine produced a slight but consistent decrease in the solid constituents of the aqueous. Decreased permeability of the blood-aqueous barrier is a possibility, but no conclusions can be drawn without further investigations.

In our experiments, physiological miosis and mydriasis produced no detectable effects on the blood-aqueous barrier, and a mydriatic (epinephrine in secondary phase) had common properties with certain miotics (mecholyl and eserine). This does not lend support to the theory proposed by Mawas[15] that alterations in the size of the pupil affect the permeability of the barrier by exposing the iris vessels. Our findings confirm the work of Adler[2] who found that variations in the protein content of the aqueous in experimental iritis produced by mustard oil were independent of changes in pupillary size.

Conclusions

1. Inulin does not pass into the aqueous across the normal blood-aqueous barrier of rabbits, or does so only in faint traces. The administration of drugs that produce permeability of the blood-aqueous barrier to inulin also results in an increase in the solid constituents of the aqueous and a decrease in the latent period required for the passage of certain crystalloid dyes of varied electric charge. A mechanical decrease in the barrier between blood and aqueous is suggested as the explanation of these phenomena.

2. Using the above criteria, the autonomic drugs can be classified according to their effects on the blood-aqueous barrier of the rabbit eye.

(a) The effects of epinephrine fall into two distinct phases. During the first hour (primary phase), there is no apparent effect on the barrier; but during the second and third hours (secondary phase), the permeability of the blood-aqueous barrier is increased.

(b) Epinephrine (secondary phase), mecholyl, eserine, and doryl have the common property of increasing the permeability of the blood-aqueous barrier. In the concentrations used, mecholyl and eserine are most effective, and doryl least. The dye studies suggest that doryl may in some way increase the permeability of the iris vessels.

(c) Pilocarpine acts as a weak miotic in albino rabbits, and it is possible that its full ocular effects cannot be obtained in these animals. Studies with inulin and dyes provide no positive evidence that pilocarpine has any effect on the permeability of the blood-aqueous barrier. However, gravimetric experiments indicate that pilocarpine has the common property with epinephrine (secondary phase), mecholyl, doryl, and eserine of increasing the total solids of the aqueous.

Atropine produces a slight decrease in the total solids of the aqueous, but without further investigation this cannot be attributed definitely to decreased permeability of the blood-aqueous barrier. The barrier remains impermeable to inulin, and the entrance of certain crystalloid dyes is not altered significantly.

3. Changes produced in the blood-aqueous barrier by the autonomic drugs are not dependent on variations in the size of the pupil.

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THE MUCOPOLYSACCHARIDE ACID OF THE CORNEA AND ITS ENZYMATIC HYDROLYSIS*

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In pursuing our work on tissue mucopolysaccharides we became interested in the polysaccharide fractions of cornea. Some of the results of our study of this subject and a discussion of some of the problems arising in connection with it are presented herewith.

Mörner[1] in 1893 isolated by aqueous extraction of cattle corneae a mucoid—that is, a protein rich in carbohydrate—which contained no sulfate. Levene and López-Suárez,[2] on the other hand, in 1918 reported the isolation of mucoitinsulfuric acid from the same source. However, many of the findings of these two authors in this field were based on rather meager evidence and could not be substantiated by other workers. In 1936 Karlberg in Upsala[3] repeated Mörner's experiments and, obtaining like Mörner a mucoid low in hydrolyzable sulfate, concluded that mucoitinsulfuric acid could not exist in any appreciable amount in the cornea. We shall return to this finding later.

In 1936 Meyer and Palmer[4] reported in a footnote to a paper on the polysaccharide from vitreous humor and umbilical cord, the isolation of a mucoitinsulfuric acid from cornea, thus confirming Levene's work. Then in 1939 a Japanese author, Suzuki,[5] claimed to have isolated from cornea a sulfuric-acid-containing polysaccharide which he said contained galactose instead of a uronic acid. This latter claim, however, was based on colorimetric methods in which galactose and glucuronic acid cannot be distinguished from each other.

In order to understand the present problem it is necessary to refer to previous work on hyaluronic acid. This high-molecular-weight polysaccharide has been isolated from vitreous humor, umbilical cord,[4] group-A hemolytic streptococcus,[6] synovial fluid,[7] fowl sarcoma,[8] and the tumor fluid of a patient with a mesothelioma of the pleura and peritoneum.[9] In all these studies an enzyme which quite specifically hydrolyzed hyaluronic acid was of immense value; with its aid it was easy to decide whether or not a viscous fluid contained hyaluronic acid and in some instances even to determine its concentration. This enzyme was first found in our laboratory in autolysates from an avirulent strain of type-II pneumococcus.[10] Later it was also demonstrated in ciliary body and iris,[11] in a group-A hemolytic streptococcus, in a strain of Clostridium welchii, and in spleen.[12]

The work on hyaluronic acid and its enzymatic hydrolysis very recently received a great impetus from the observation by Chain and Duthie[13] that the "spreading factor" of testis diminished the viscosity of synovial fluid and vitreous humor, two fluids containing hyaluronic acid as their viscous components. Shortly afterward we confirmed the observations of the English authors and found further that testis extracts hydrolyzed pure hyaluronic acid just as our pneumococcus preparations did, although the enzymes differed in many respects, including pH optimum.[14] Another good

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This work has been supported in part by a grant from the John and Mary R. Markle Foundation.

source of both "spreading factor" and hyaluronidase is leech extract, as recently demonstrated by Claude[15] and in our Institute.[16]

It might be mentioned briefly here that the "spreading factor" found by Duran-Reynals[17] causes the spreading of substances injected intracutaneously, such as India ink, certain dyes, bacterial toxins, and tumors. It also influences capillary permeability as demonstrated by Duran-Reynals[18] and by Claude.[19] There seems to be no question that this spreading factor is of great bacteriological and probably physiological significance. For example, it was found in only one of five group-A hemolytic-streptococcus strains tested, and this strain was originally isolated from a fatal case of erysipelas. The "spreading factor" and hyaluronidase are not identical; in a paper in collaboration with Drs. Hobby and Dawson[20] it is pointed out that all fractions showing hyaluronidase action also show spreading properties but that spreading may be found, especially in some bacterial extracts, without hyaluronidase action.

Now let us return to the cornea polysaccharide. We employed for its isolation both alkaline hydrolysis and more gentle methods such as extraction with 50-percent urea solution at a pH of about 9.

In the earlier procedure the corneae were treated either with 10 volumes of 10-percent $Ca(OH)_2$ at room temperature or with normal NaOH at 37°C., until the corneae had largely disintegrated. After acidification with glacial acetic acid and fractionation with alcohol, the material was treated similarly to the method for preparation of chondroitinsulfuric acid from cartilage.[21] In many instances preparations thus obtained proved to have only a purity of about 50 percent.

Lately we have isolated the cornea polysaccharide by a method avoiding the use of strong alkali. The corneae of 200 eyes were dissected, washed thoroughly with water, and ground finely in a meat chopper. To the mass 600 c.c. of 50-percent urea was added and enough N NaOH (about 5 c.c.) was added to give a pH of about 9. The mixture was allowed to stand at room temperature for about three weeks, centrifuged, and twice more extracted for a few days with 300 c.c. 50-percent urea. The solution was diluted four times with water and acidified with 20-percent acetic acid. The precipitate was washed with water, and the protein salt dissolved in 10-percent $CaCl_2$ in slightly alkaline solution. This mixture is shaken with chloroform-amyl alcohol mixture as described in earlier papers.[4] The clear fluid is first precipitated with 2 volumes of alcohol, dissolved in water with neutralization, treated in one normal acetic-acid solution with Lloyd's reagent, and again precipitated by 2 volumes of alcohol. The precipitate is extracted with small amounts of water and the aqueous solution precipitated by glacial acetic acid. After washing with alcohol, acetone, and ether, and drying *in vacuo*, a white fibrous material is obtained.

In table 1 the analytical data of one such preparation are given. We have obtained a number of other preparations giving similar results. It is obvious from these data that we are dealing with a substance containing one mol each of a hexosamine, of a hexuronic acid, of acetyl, and of sulfuric acid; that is, a substance having the general composition of a chondroitin or mucoitinsulfuric acid. The amino sugar was isolated from one preparation as the hydrochloride and proved to be glucosamine on the basis of analysis and rotation (N found 6.35 percent, $[\alpha]_D$ + 72.5 degrees; N theory 6.46 percent, $[\alpha]_D$ of pure d-glucosam-

TABLE 1

ANALYSIS OF POLYSACCHARIDE ACID OF CORNEA

	Nitrogen	Hexosamine	Uronic Acid	Acetyl	Sulfur	Acid Eq. Wt.	Moisture	Ash	$[\alpha]_D$ neutralized
Percent	2.63	31.8	35.0	9.60	5.03	560	5.06	10.8	−51°
Eq. per Eq. Wt.	1.05	0.99	1.01	1.25	0.88				

ine-HCl + 72.5 degrees). The specific rotation of the cornea polysaccharide was —51 degrees. When calculated on the basis of an ash and sulfate-free compound, the rotation becomes quite similar to that of hyaluronic acid, which varies from —65 degrees to —75 degrees.

The yield from 200 corneae varied between 150 ($CaCl_2$ method) and 400 mg.

TABLE 2

HYDROLYSIS BY PNEUMOCOCCUS ENZYME

	Percent Hydrolysis		
	2 hrs.	20 hrs.	45 hrs.
I Cornea polys.	15	53	55
II Cornea polys.	9	37	44
Hyaluronic acid	44	79	87

(by alkaline digestion). Considering unavoidable losses during preparation, the latter figure may be still somewhat too low. The average dry weight of our cattle cornea was 0.11 gm., giving a polysaccharide concentration of at least 1.82 percent. This figure would become greater if calculated only on the basis of the weight of the substantia propria (see below).

Solutions of the cornea polysaccharide, furthermore, are quite viscous and are hydrolyzed by the pneumococcus enzyme. In table 2 the hydrolysis of equivalent concentrations of cornea polysaccharides and hyaluronic acid by a pneumococcus enzyme is shown. It can be seen that the hydrolysis of the cornea polysaccharides is considerably less than that of hyaluronic acid. This is due to the stronger acidity of the cornea compound as compared to that of hyaluronic acid itself. In a previous study[12] we synthesized sulfuric-acid esters of hyaluronic acid by sulfonating with pyridinium sulfonic acid and chlorsulfonic acid in pyridine. Their hydrolysis by the pneumococcus enzyme was similarly delayed. The testis enzyme likewise hydrolyzed the cornea polysaccharide at about the same rate as the pneumococcus enzyme, though again more slowly than it hydrolyzed hyaluronic acid.

From the analysis, from the rotation, and from its enzymatic hydrolysis we can conclude that the cornea polysaccharide is a natural monosulfuric-acid ester of hyaluronic acid. We might mention here that the mucoitinsulfuric acid which we isolated previously from gastric mucosa[22] differs markedly from the cornea polysaccharide in its rotation and is completely resistant to the pneumococcus enzyme. On the basis of these differences it

TABLE 3

HYDROLYSIS OF HYALURONIC ACID BY PRESS JUICE OF RABBIT CORNEAE

	Increase in Reducing Values (Calculated as Glucose)	
	16 hrs.	40 hrs.
	mg. per c.c.	mg. per c.c.
0.5 c.c. Cornea extract	0.275	0.340
0.1 c.c. Cornea extract +0.4 c.c. saline	0.050	0.050

0.5 c.c. of a 1-percent solution of hyaluronic acid was incubated at 37° with cornea extract, in the presence of toluol, at pH 5.9. Reducing values were determined on 0.2 c.c. by the ceric sulfate method.[24]

may be assumed to have quite a different structure.

The findings of Mörner and of Karlberg of a "mucoid" almost free of sulfuric acid need to be discussed. These authors extracted the corneae with water. Sulfuric-acid esters of the nature of the cornea polysaccharide form very stable protein salts which are water insoluble. Either strong alkali or peptizing agents such as strong urea solution or concentrated calcium-chloride solutions have to be used to bring the protein complexes into solution. In our own experiments the corneae were washed repeatedly with water to remove any soluble components. Whether these washings removed a true sulfate-free mucoid was never investigated, but such mucoids occur in many fluids and cells and may be present in the epithelium.

The source of the hyaluronosulfuric acid, as we might call the cornea polysaccharide, must be the substantia propria of the cornea. The metachromatic staining with toluidine blue indicates this since only sulfuric-acid esters give such staining. In a report by Jorpes, Holmgren, and Wilander,[23] this is beautifully illustrated. Only the substantia propria has taken the reddish stain while epithelium and endothelium remain pure blue.

So far as we know at present, the sulfuric-acid ester of hyaluronic acid occurs only in the cornea. From the sclera, which resembles the cornea in its large amount of collagen, we were unable to obtain any polysaccharide. Levene and López-Suárez[2] claimed to have obtained chondroitinsulfuric acid from the sclera but did not report the yields. We were unsuccessful in several attempts to repeat this experiment. From skin we recently obtained a polysaccharide mixture. About half of it is apparently hyaluronic acid, which was hydrolyzed by the pneumococcus enzyme at the same rate as hyaluronic acid from other sources. The other half was a sulfuric-acid ester of a polysaccharide which was completely resistant to the pneumococcus enzyme. We have so far not identified this second component.

Finally, we might be permitted to speculate on some problems which we believe to be connected with this polysaccharide and its enzymatic hydrolysis. Our working hypothesis is that the polysaccharide is intimately connected with corneal transparency and with the absence of blood vessels from the cornea. In support of this hypothesis are the following facts: (1) Hyaline cartilage which, like the cornea, is free of blood vessels, contains the very similar carbohydrate sulfuric-acid ester, chondroitinsulfuric acid. (2) In hyaline and amyloid degeneration a sulfuric-acid-containing polysaccharide of yet unknown nature likewise seems to be present. (3) In some experiments which we have undertaken with Dr. Thygeson, and more extensively with Dr. Sallman, the intracorneal injection of enzyme, at least that prepared from pneumococcus, caused vascularization of the cornea, while inactivated enzyme in most instances caused only a transient reaction; the results with testis enzyme and leech enzyme were not so clear cut; (4) An enzyme which hydrolyzes hyaluronic acid and causes a considerable diminishing of the viscosity of a hyaluronic acid-containing fluid was demonstrated to be present in a low concentration in the press juice of normal rabbit corneae.

Twenty rabbit corneae were subjected in a hydraulic press to a pressure of 15,000 to 20,000 lbs. per sq. in. The collected turbid fluid, about 1.2 c.c., was incubated with hyaluronic acid as shown in table 3.

In another experiment 0.1 c.c. cornea extract and 0.1 c.c. saline, respectively, were incubated at 37 degrees in the pres-

ence of toluene with 1 c.c. of tumor fluid each for 23 hours. The viscosity of the fluid containing the cornea extract was reduced by 36.4 percent against the saline control.

Thus it may be possible that various lesions produce an increase in enzymatic activity, this in turn leading to a loss of the polysaccharide and consequent vascularization and turbidity. The protein complexes of hyalurono-sulfuric acid itself might be considered from a purely physical point of view as excellently suited to form the basis of transparent media. They form stable gels, containing large amounts of water and thus having a refractive index very similar to that of the surrounding medium. The hyaluronidases bring about the rapid breakdown of these gels. It is fully appreciated that the role of such enzymes and of the polysaccharides has to be tested by further experiments.

Summary

From cattle corneae, a polysaccharide acid has been isolated which contains a hexosamine, a hexuronic acid, acetyl, and sulfuric acid in equimolar ratio. The hexosamine was isolated and characterized as glucosamine. Thus the acid has the composition of a mucoitinsulfuric acid. From the rotation and the enzymatic analysis by enzymes prepared from pneumococcus and from testis, it has been possible to characterize the polysaccharide further as a sulfuric-acid ester of hyaluronic acid. As far as we know at present, it occurs only in the cornea, the mucoitinsulfuric acid from gastric mucosa being quite different as to properties. From the metachromatic staining of the substantia propria, it is concluded that this corneal layer contains the acid.

The hypothesis that the polysaccharide is connected with corneal transparency and the absence of blood vessels from the cornea are discussed.

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Discussion

Dr. Frederick H. Verhoeff: I should like to ask the essayist if the stroma of the sclera gives the same sort of staining that the cornea does.

Dr. Meyer: In the article by Jorpes, Holmgren, and Wilander, which I mentioned earlier in the paper, the statement is made that the sclera of *man* shows no signs of any metachromasy. In bovine sclera the authors find some scattered "mast cells" which show metachromatic granules. They claim that these mast cells carry heparin, which as a carbohydrate polysulfuric acid ester strongly takes the metachromatic stain. The work of the Swedish authors was undertaken to test for the origin and occurrence of heparin. We have tested the cornea polysaccharide for heparin activity and found it very weakly active. Furthermore, heparin is completely resistant against our enzymes, so that we are certain we were not dealing with heparin.

DARK ADAPTATION AND DIETARY DEFICIENCY IN VITAMIN A*†

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Although a disturbance of the sensitivity of the dark-adapted retina (night blindness) was noted centuries ago, and in spite of the fact that frequent observations of its associations with malnutrition were made during the latter part of the nineteenth and early years of the twentieth centuries,[1, 2, 3, 4] no etiologic relationship was established until Holm,[5] in 1925, demonstrated that rats became night-blind when fed for a few weeks on a diet deficient in vitamin A. The work of Holm has been verified by several investigators.[6, 7] Other experimental approaches to the problem have demonstrated that the concentration of visual purple in the retinas of frogs, rats, and dogs suffering from severe avitaminosis A is very low and, on occasion, visual purple may not be present.[8] Various investigations have shown that persons with severe cases of night blindness may be benefited or may have the normal levels of sensitivity restored by the addition of vitamin A to the diet.[9, 10] So far as is known, vitamin A and its precursors are the only dietary constituents that will produce these curative effects.[11] As the result of these different types of researches, the association of vitamin A with the visual cycle has been established, not only indirectly by the occurrence of night blindness with deficiency of vitamin A but also by the direct chemical identification by Wald,[12, 13] in 1935, of vitamin A and the carotenoid retinene in the retina.

After the establishment of vitamin A as a factor in visual adaptation, it seemed logical to employ the properties of vision in the detection of early stages of vitamin-A deficiency. Tests of this character were made by Edmund and Clemmesen,[14] with discrimination of visual intensity as an index. At about the same time, clinical

* Read before the Association for Research in Ophthalmology, New York, June 11, 1940.

† Portion of the material submitted by Dr. L. F. Steffens to the faculty of the graduate school of the University of Minnesota in partial fulfillment of the requirements for the degree of Master of Science in Ophthalmology.

‡ Formerly a fellow in Ophthalmology, The Mayo Foundation, and now of the Medical Associates, Dubuque, Iowa.

interest in the determination of dark adaptation as a method of detecting subclinical states of vitamin-A deficiency was stimulated by the investigations of Jeans and Zentmire[15, 16] who, in 1934 and 1936, reported that, by means of an adaptometer, they found a disturbance of dark adaptation in 21 percent of a group of 213 children in a children's hospital in Iowa. About a half of the children who showed relatively low rates of dark adaptation and, therefore, relatively high values of threshold intensities, were placed on a high-vitamin diet including cod-liver oil and, after a period averaging 12 days (from four days to six weeks), all were reported to have demonstrated an improvement in dark adaptation. Other investigators[17, 18, 19] have concluded that the incidence of vitamin-A deficiency is likely to be high if photometers and the standard of normal thresholds assumed by Jeans and Zentmire are used and that, although some relationship may exist between the photometric readings and the state of vitamin-A nutrition, the relationship is not close enough to warrant the use of the test as a means of diagnosing subclinical vitamin-A deficiency.[20, 21, 22] Furthermore, it has been difficult in many cases to correlate the variations in photometric determinations of dark adaptation and the content of vitamin A in the diets.

Because of the disparity of findings and conclusions, and because of the various criticisms that had been made regarding experimental ensembles and techniques, we undertook an investigation, covering the period of time between June, 1938, and February, 1939, to determine whether vitamin-A deficiency, as evidenced by photometric readings on a rather simple, readily operated and controlled adaptometer which we constructed, could be produced in three normal individuals. If vitamin-A deficiency could be demonstrated, we were interested in determining whether there was a loss of sensitivity in cone vision (macular area) as well as in rod vision (peripheral area). Furthermore, if vitamin-A deficiency could be demonstrated definitely in either rod or cone vision, or both, through appreciable changes in the course of dark adaptation, we should be concerned thereafter with the matter of the restoration to normal thresholds by diets controlled as to the intake of vitamin A.

Standard conditions and apparatus

Apparatus. Two adjoining rooms (a and b in figure 1) were made light proof and so arranged that the person under test, the small light with red filter (C) which served as a fixation target, and the area (A), which, on illumination, acted as the source of retinal stimulus were placed in one room. The second room contained the optical bench (D) and sliding head carrying a small lamp (E) which, on movement toward the subject, caused an increase in the intensity of the light that fell on the retinal-stimulus target (A). The threshold intensities, in micromillilamberts, were determined by previous calibration of the source of light at a known distance from the stimulus target and through the use of the law of inverse squares. A diagrammatic sketch of the arrangement of apparatus for obtaining threshold intensities is given in figure 1.

Method of test. In general, and unless stated to the contrary, in the investigations that are reported here, the subject's right eye (the left eye being occluded) was light adapted for three minutes by gazing upon a white screen (B, fig. 1) with a uniform brightness of 160 apparent foot-candles. At the end of the period of light adaptation, the adapting source was turned off, the subject then directed

his attention to the fixation light (C) and the examiner slowly moved the light source (E) toward the subject so as to increase the intensity of illumination on the stimulus target (A). At the moment the light on the target was seen, the subject indicated the fact by a suitable signal to the examiner. Records were then made of the time which had elapsed since the onset of dark adaptation, the position of the lamp (E) on the optical bench (D),

$$I = k \frac{I_1 F P^2}{D^2}$$

in which I_1 is the brightness of the target (A) in micromillilamberts at a specified distance (D_1) of the light source from the target, F the value of light transmission of the filter used, P the pupillary diameter, and D the position of the light (E) on the optical bench.

Diet. The intake of vitamin A of the

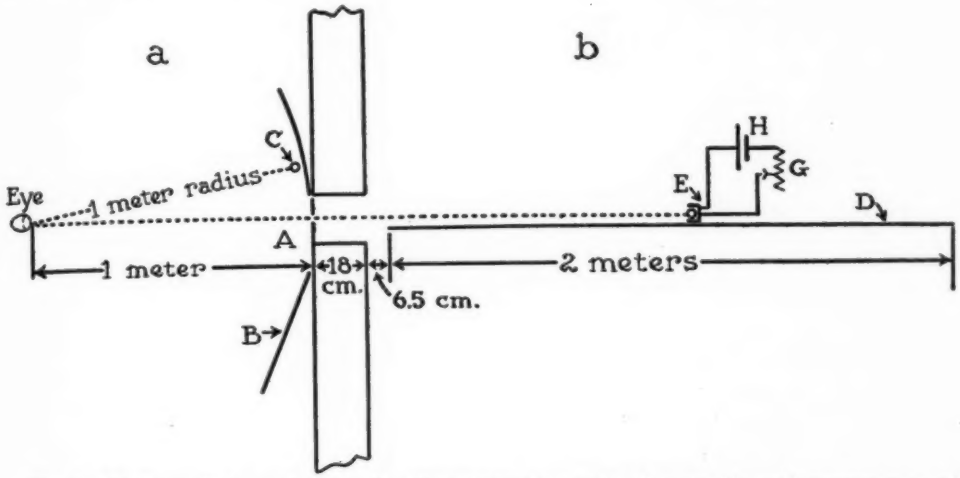

Fig. 1 (Steffens, Bair, and Sheard). Diagrammatic sketch of ensemble and arrangement of apparatus for obtaining the values of the threshold levels during the course of dark adaptation; A, retinal-stimulus target; B, source for light adaptation; C, small fixation light with red filter; D, photometer; E, light source for retinal-stimulus target.

and the value of light transmission of any filter that might be used in connection with the photometric determinations in order that the retinal sensitivity to light might be calculated.

The pupil of the eye under test was dilated with a 1-percent solution of euphthalmine hydrochloride. The diameter of the pupil was measured by means of the Moss[23] modification of the Broca pupillometer at the conclusion of each series of determinations of the threshold values. All calculations of the intensity of the light thresholds (reduced to a standard pupillary diameter of 5 mm.) were made according to the formula

experimental subjects was calculated from the vitamin content of foods given by Daniel and Munsell.[24] Analyses of the ingredients of the food and vitamin contents during the period of dietary deficiency in vitamin A showed that the intake of protein, calcium, phosphorus, iron, and vitamins (other than vitamin A) was adequate. The daily intake of vitamin A was restricted to 100 to 300 international units.

Experimental results concerning light thresholds

Figure 2 contains a set of data showing the course of dark adaptation when the

macula (curve 1) and a region 10 degrees above the macula (curve 2), respectively, are stimulated in areas with diameters which subtend 0.33 degree at the nodal point of the eye. These data are representative of the findings obtained on all subjects and were taken prior to the period of vitamin-A-deficient diets. Determinations of light sensitivity during dark adaptation were made at intervals of one-half minute to two minutes; arrangements were made whereby alternate readings on macular and paramacular areas could be obtained; intermittent light stimulus was introduced. These variations and modifications produced minor changes only in the values of the threshold intensities.

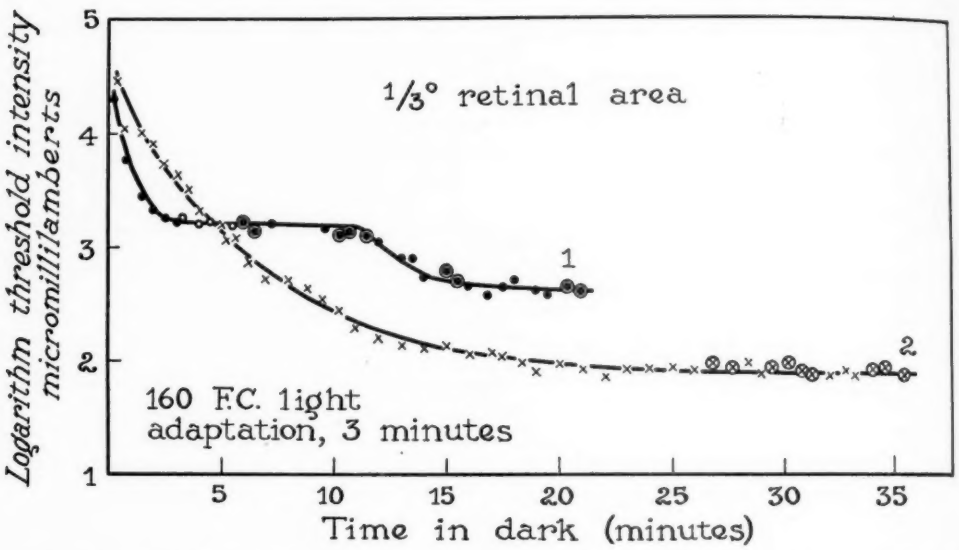

Fig. 2 (Steffens, Bair, and Sheard). Representative sets of data showing the course of dark adaptation for the macula (curve 1) and an area 10 degrees above the macula, after light adaptation to 160 foot-candles for three minutes. The retinal-stimulus area is one-third degree. The points marked with either a dot (curve 1) or cross (curve 2) within a circle are readings taken with an intermittent-light stimulus.

In figure 3 are shown composite curves of the dark adaptation of one subject using a 0.33-degree test source after an adaptation to 160 foot-candles for three minutes. The curves of this illustration cover a period of 190 days on a diet deficient in vitamin A and give the values of the brightness of light (plotted on a logarithmic scale) necessary to render the test area visible, both at the macula and 10 degrees above the macula, after 1, 5, 10, 15, and 20 minutes, respectively, of dark adaptation. Variations of the threshold values, occurring at the end of any period of dark adaptation during the course of these tests, are in the same direction (either increase or decrease in light intensity) for both the macular and paramacular regions. There was less variation in the values of the light thresholds at the macula after 10 minutes of dark adaptation than at any other point of the 20-minute test period. The most constant paramacular threshold was obtained after 20 minutes of dark adaptation. The same statement is applicable to data obtained on another subject on whom the largest number (21) of complete tests were made.

Figure 4 gives, in graphic form, a

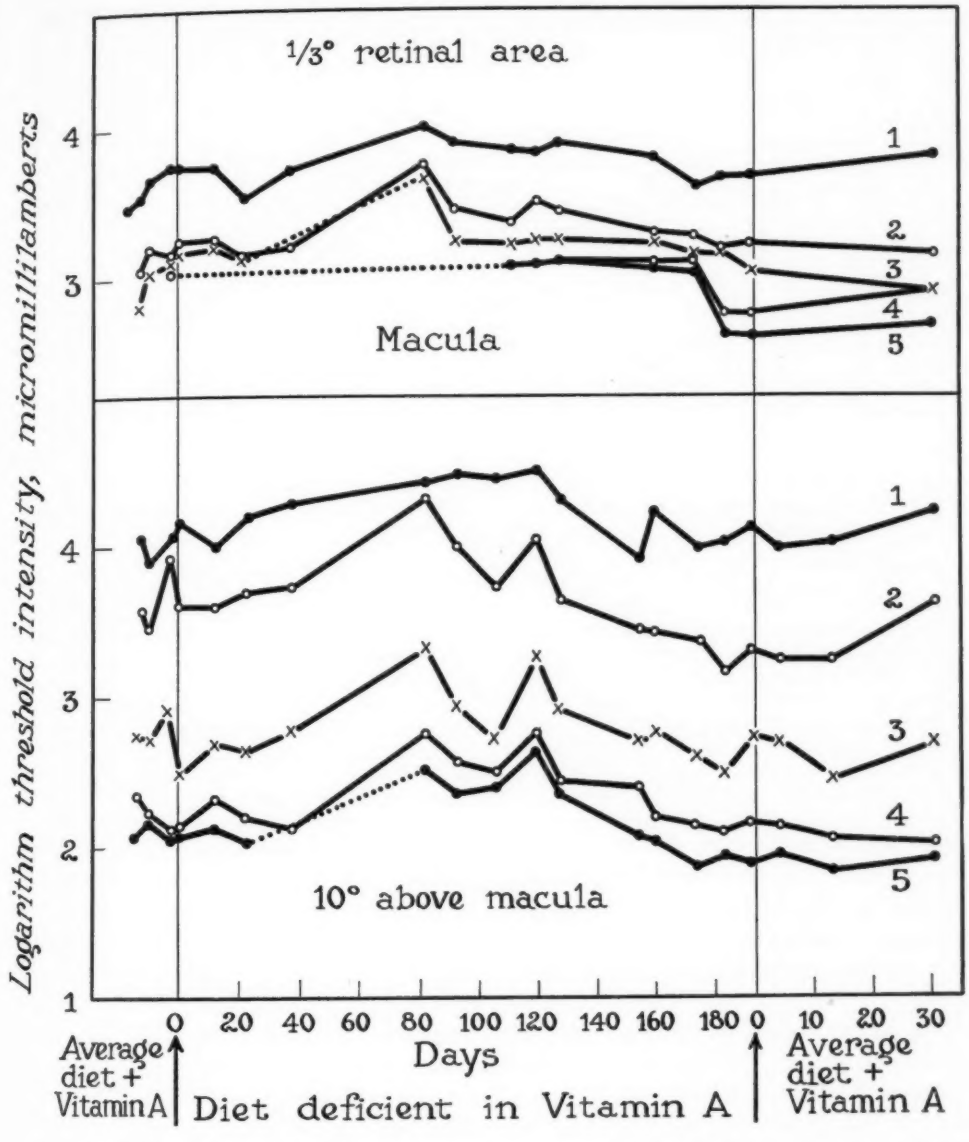

Fig. 3 (Steffens, Bair, and Sheard). Composite curves of dark adaptation using a one-third-degree retinal-stimulus area, after a previous light adaptation for three minutes to 160 foot-candles, for the macular area and for an area 10 degrees above the macula. The curves 1, 2, 3, 4, and 5, as plotted for both macular and paramacular areas, show the values of the calculated threshold levels at 1, 5, 10, 15, and 20 minutes, respectively, after the commencement of dark adaptation for one of the subjects tested and on each of the days indicated on the chart.

résumé of the values of the threshold stimuli (plotted as logarithms of the threshold brightness in micromillilamberts) for the three subjects (two of whom were on a diet deficient in vitamin A for 160 and 190 days, respectively), using a 0.33-degree stimulus area and a previous light adaptation of 160 foot-candles for three minutes. These composite curves give the values of the light

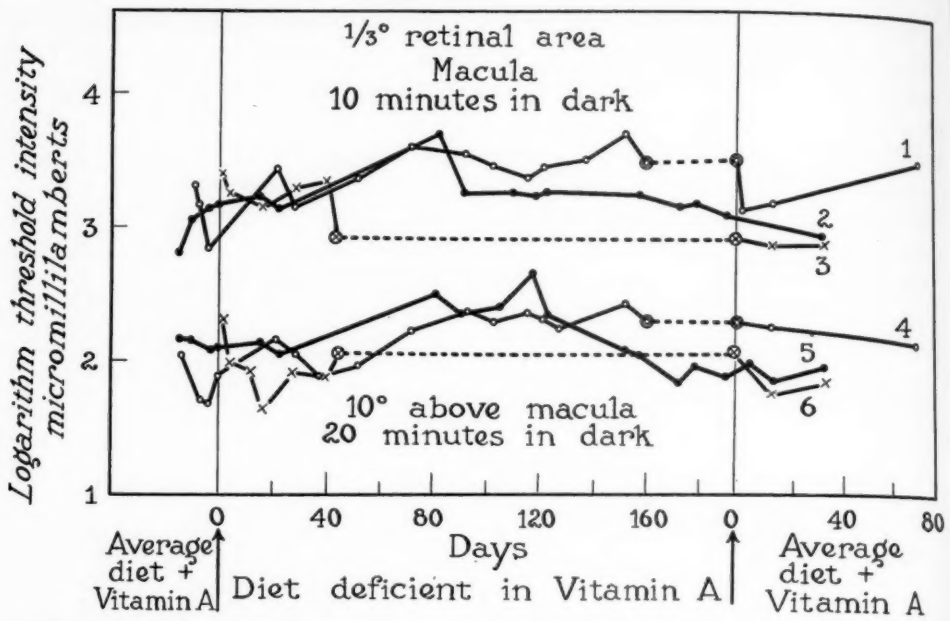

Fig. 4 (Steffens, Bair, and Sheard). Composite curves of the courses of dark adaptation, using a one-third-degree stimulus area and a previous light adaptation of 160 foot-candles for three minutes, for the macula (curves 1, 2, and 3) and for an area 10 degrees above the macula (curves 4, 5, and 6), during the course of the investigation of three subjects on a diet deficient in vitamin A and after the return to normal diets. Curves 1 and 4 (subject 1), curves 2 and 5 (subject 2), and curves 3 and 6 (subject 3). The threshold levels at the macula (curves 1, 2, and 3) were obtained after 10 minutes of dark adaptation and those for an area 10 degrees above the macula (curves 4, 5, and 6) were obtained after 20 minutes of dark adaptation.

thresholds at the macula (after 10 minutes of dark adaptation) and at an area 10 degrees above the macula (after 20 minutes of dark adaptation) on various days during the period of experimentation.

The data plotted in figures 3 and 4 show that, during the first three months that subjects 1 and 2 were on the deficient diet, the dark-adaptation thresholds of the macular and paramacular (10 degrees above the macula) regions were elevated only 0.5 log unit approximately. However, this is not a change of sufficient magnitude to warrant a conclusion that there is any evidence of vitamin-A deficiency. Furthermore, the thresholds, instead of showing an increase in values throughout the course of the dietary period, tended to decrease and to assume the same levels of threshold values as had been observed when the subjects were initially on a normal, adequate diet. Also, after the cessation of the deficient diet and during the period of normal diets, supplemented with 80,000 units of vitamin A for 70 days in the case of one subject, the level of values of the light thresholds was not affected. It appears, therefore, from these and other data obtained by the use of different sizes of retinal areas of stimulation (figs. 5 and 6) and various modifications in experimental procedure, that we obtained no evidence from photometric measurements to indicate that any significant changes in light thresholds had been produced by any alterations in diet, that is, either by drastic reductions in vitamin-A intake or by the daily ingestion of several thousand units of vitamin A added to an adequate diet.

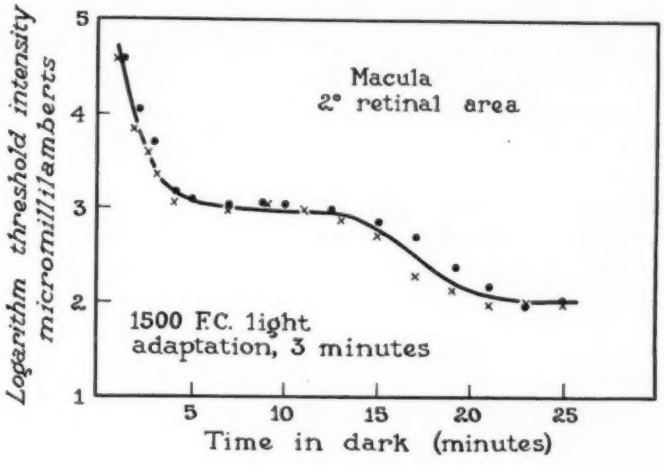

Fig. 5 (Steffens, Bair, and Sheard). Curve showing the course of dark adaptation at the macula, using a large (2-degree) stimulus area and a high (1,500 foot-candle) light adaptation for three minutes. The crosses (×) represent the values obtained when the subject had been on a diet deficient in vitamin A for 183 days; the dots (•) show the values obtained 34 days after the resumption of normal diets supplemented with vitamins (80,000 units daily of vitamin A).

Furthermore, during the course of these investigations we made use of the biophotometer in measuring the light thresholds of the three subjects. The manner of making determinations of thresholds was modified from that described by Jeans. Instead of using both eyes, the left eye was occluded and the right pupil was dilated with euphthalmine hydrochloride. The left upper spot of the quincunx was used as the fixation target and a signal was given when the observer first saw the center spot or area of the quincunx. The data of table 1 and figure 7 show that the light thresholds and courses of dark adaptation are very nearly the same for subjects 1 and 2 and, furthermore, that the threshold values are comparable to, and in many cases identical with, the values obtained by the use of our experimental ensemble. Hence it may be concluded that differences in instrumentation and essentials of experimental procedure are not responsible for the results which we have obtained and which are at variance with the conclusions of a number of other investigators.

Dermatologic findings

A study of the skin of one subject furnished evidence to indicate that the earliest sign of vitamin-A deficiency is

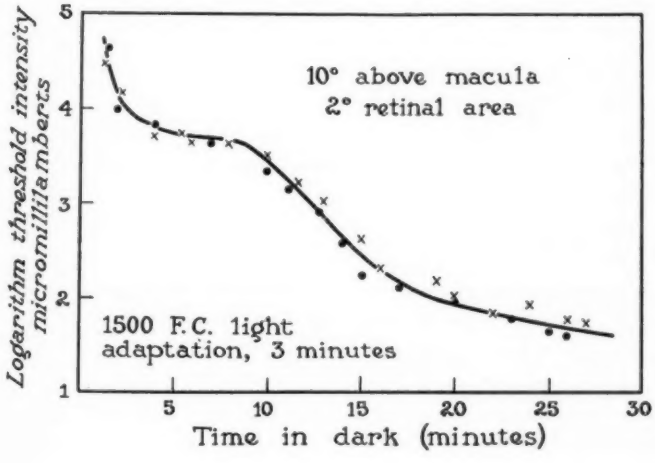
Logarithm threshold intensity micromillilamberts
10° above macula
2° retinal area
1500 F.C. light adaptation, 3 minutes
Time in dark (minutes)

Fig. 6 (Steffens, Bair, and Sheard). Curve showing the course of dark adaptation in an area 10 degrees above the macula, using a 2-degree retinal-stimulus area after a previous light adaptation to 1,500 foot-candles. The crosses (×) represent the various threshold levels obtained when the subject had been on a diet deficient in vitamin A for 183 days; the dots (•) show the values obtained 34 days after the resumption of normal diets supplemented with vitamins (80,000 units daily of vitamin A).

TABLE 1

COMPARISON OF DATA OBTAINED BY THE BIOPHOTOMETER AND BY OUR ADAPTOMETER AND PHOTOMETRIC ENSEMBLE ON A SUBJECT WHO HAD BEEN ON A DIET DEFICIENT IN VITAMIN A FOR 160 DAYS

Biophotometer

Time in Dark (minutes)	Dial Reading	Intensity, Light Threshold (millifoot-candles)	Intensity, Light Threshold (micromillilamberts)	Logarithm, Intensity of Light Threshold (corrected to 5-mm. pupil)
1	18	1.140	2404	3.38
4	20	0.980	2066	3.32
6	31	0.463	976	2.99
8	49	0.132	278	2.45
10	56	0.081	170	2.23

Adaptometer (S, B, and S)

Time in Dark (minutes)	Filter (percent transmission)	Distance of Light Source on Photometer	Threshold Intensity (micromillilamberts) corrected to 5-mm. pupil	Logarithm, Intensity Light Threshold
1	No filter	29	17400	4.24
4	No filter	122	2170	3.34
6	10	51	890	2.89
8	10	69	339	2.53
10	10	124	195	2.29
12	10	143	159	2.20
15	10	158	132	2.12
20	1	44	97	1.98

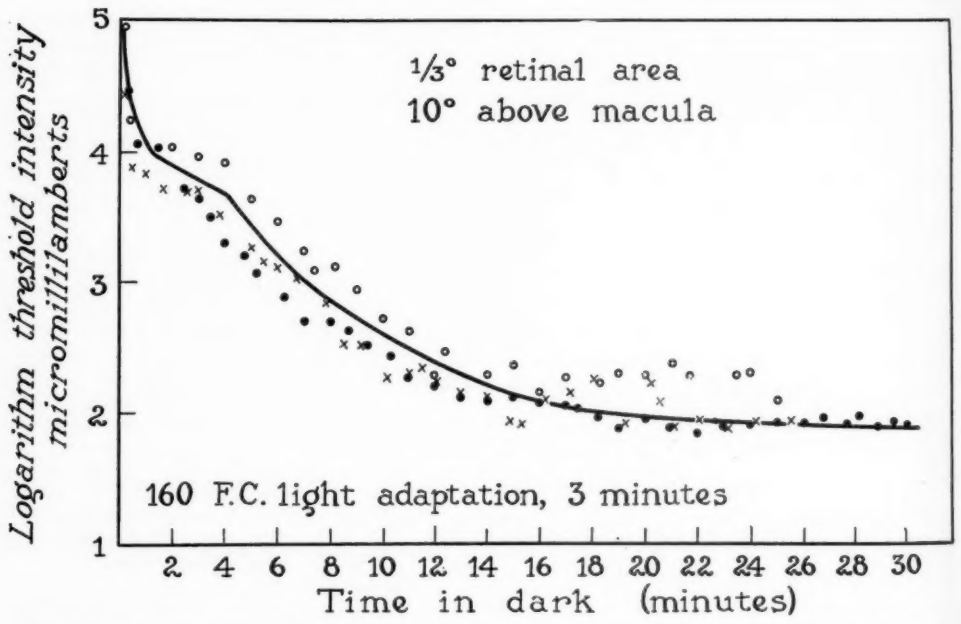

Fig. 7 (Steffens, Bair, and Sheard). The courses of dark adaptation in an area 10 degrees above the macula of three subjects used in these tests after 28 days (subject 3), 160 days (subject 2), and 180 days (subject 1) on a diet deficient in vitamin A. Plots show subject 1 (°), subject 2 (•), and subject 3 (×).

not always to be detected by tests on the levels of light sensitivity but by microscopic examinations of sections of the skin. This conclusion is in agreement with the clinical experience of certain other investigators[25, 26] in this field.

A biopsy of the skin of the extensor surface of the right upper arm was performed on one subject after he had been on the vitamin-A-deficient diet for 189 days. There were no macroscopic lesions of the skin nor symptoms of a dermatologic disorder present at that time. Microscopic examinations of the skin (made by Dr. H. Montgomery of the Section on Dermatology and Syphilology, The Mayo Clinic) showed the following changes in the skin (fig. 8):

Epidermis. 1. There is relative and absolute hyperkeratosis; keratotic plugging is present in all the hair follicles and also independent of the follicles. 2. Acanthosis and intracellular edema are present in moderate amounts in the prickle-cell layer. 3. Pyknosis of some of the nuclei and an increased amount of melanin are present in the basal-cell layer. 4. Sebaceous glands are not present.

Upper cutis. A mild perivascular lymphocytic infiltration is present. There is some edema and homogenization of the elastic tissue and of the collagen fibers.

Another biopsy of the skin of the extensor surface of the left upper arm was performed 17 days after the first biopsy or 16 days after the subject had been placed on a normal diet supplemented by 80,000 units of vitamin A daily. Examination of the section of the second biopsy specimen (fig. 9) showed that the skin was essentially normal except for occasional keratotic plugs in the hair follicles.

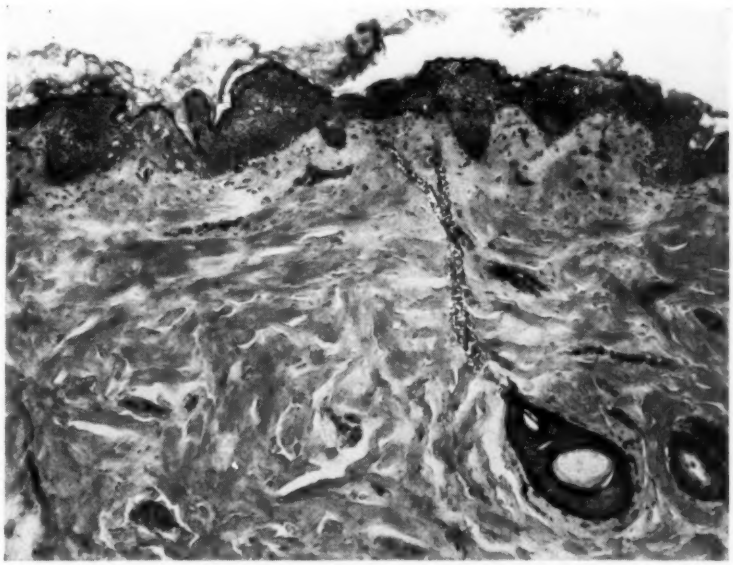

Fig. 8 (Steffens, Bair, and Sheard). Photomicrograph (×80) of a section of the skin of one subject taken after a period of 189 days on a diet deficient in vitamin A. Changes in the epidermis are relative and absolute hyperkeratosis, acanthosis, vacuolization of cells, and pyknosis of some basal cells. In the cutis, there is homogenization of the elastic and collagenous fibers and perivascular infiltration. The sebaceous glands have atrophied.

The changes in the skin, as shown in figure 8, are similar to those described by various investigators who were concerned with lesions produced by vitamin-A deficiency. The presence of hyperkeratosis, keratotic plugging of hair follicles, acanthosis and intracellular edema seen in the section of skin taken after six months on a low-vitamin-A diet and the absence thereof in the skin (fig. 9) after the ingestion of large amounts of vitamin A for a period of two to three weeks are in support of investigations indicating that skin lesions may be the first signs

of vitamin-A deficiency in many instances.

Dietary avitaminosis A

The curves given in figure 10 show the changes in the levels of the light thresholds, at the macula and in an area 10 degrees above the macula, which were obtained from a patient who had been on a diet deficient in calories, proteins, and vitamins for about nine months prior to examination at The Mayo Clinic. The patient gave a history of severe headaches associated with nausea and vomiting over a period of four years. Her dietary deficiency was brought about by special diets which had been prescribed and which she had depleted further by voluntary restriction. The course of dark adaptation in both the macular and paramacular regions (curves 1, fig. 10) shows that the levels of light thresholds are at least 1 log unit (or a factor of 10 in terms of actual light intensity) above the normal level (curves 3, fig. 10 or curves 1 and 2, fig. 2).

Subsequent to the initial determinations of the course of dark adaptation the patient was placed on well-balanced diets supplemented by large doses daily of vitamin concentrates. During the first eight days on the high-vitamin regimen, there was no change in response in either the macular or paramacular regions, as is indicated by the readings marked (x) on curves 1, figure 10. Four months later, during which the adequate diet was maintained, the measurements of light thresholds gave the data shown in curves 2. There is a reduction of about 0.8 log unit in the paramacular area and approximately 0.5 log unit at the macula. The tendency toward restoration to normal threshold levels is greater in paramacular areas. In other clinical cases evidencing abnormally high light thresholds, we have found that there may be a restoration to normal values in the light thresholds of the peripheral retina accompanied by only partial restoration of light thresholds of the macula.

The case which we have cited shows evidence of visual dysaptation and rather slow subsequent return to normal levels after high vitamin-A intake. In other instances, however, the abnormally high

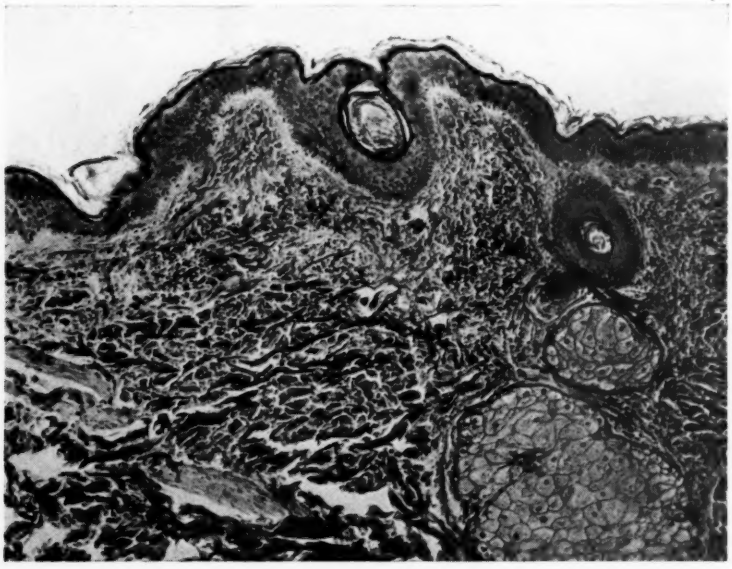

Fig. 9 (Steffens, Bair, and Sheard). Photomicrograph (×80) of a section of the skin of the same subject as shown in figure 8 and taken after 16 days on normal diets supplemented with 80,000 units daily of vitamin A. Skin is normal except for occasional keratotic plugging in the epidermis.

levels may be maintained and little or no change be produced by adequate diets continued for several months. And again, somewhat in disagreement with both types of findings, are those cases in which little change is found in light thresholds during the first week to possibly three weeks, followed by restoration of light thresholds to normal levels in the course of the subsequent 24 to 48 hours.

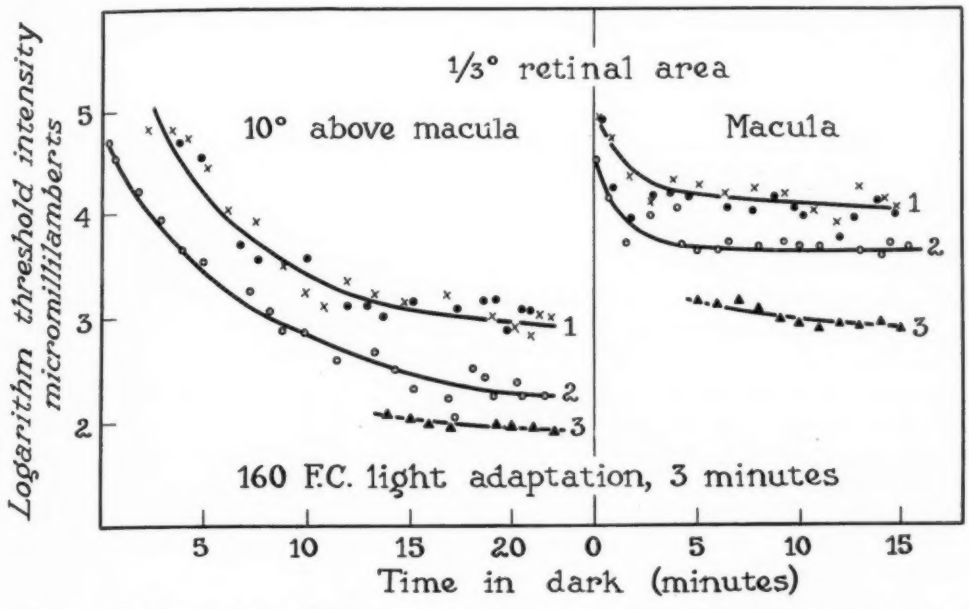

Fig. 10 (Steffens, Bair, and Sheard). Curves showing the course of dark adaptation in a subject who was poorly nourished and who had been placed on a restricted diet for many months. The areas investigated were the macula and 10 degrees above the macula, using a one-third-degree stimulus area after a previous light adaptation to 160 foot-candles for three minutes. Curves marked 1 (macular and paramacular regions) show the values of the threshold levels as initially obtained (indicated by •), and as obtained eight days later (indicated by ×) after the subject had been placed on normal diets supplemented with high daily intake of vitamin A. Curves marked 2 (for both macular and paramacular areas) show the values of the light thresholds of the subject after being placed on an adequate diet with large daily intake of vitamins over a period of about four months. Curves marked 3 contain representative data of a normal individual. After four months on a normal diet, richly supplemented with vitamins, there is a reduction in the threshold levels (at the 20-minute point of the course of dark adaptation) of about 0.8 log unit (sixfold) in the paramacular region chosen and approximately 0.5 log unit (threefold) at the macula.

Dark adaptation in follicular hyperkeratosis

Table 2 contains data on the values of the threshold levels in a case of follicular hyperkeratosis. Although the patient did not give a history of night blindness, it seemed desirable to determine the courses of dark adaptation because of the extensive keratinization of the follicular orifices. The initial threshold values for any specified time during the course of dark adaptation were found to be from 0.4 log unit to 0.85 log unit higher than the average values which were obtained from 50 different sets of determinations on three normal subjects. Subsequent to the initial determinations of dark adaptation, the diet of the patient was fortified with foods of high vitamin content, including fats. Carotene in oil was given orally. Inunctions of cod-liver oil, about

150 c.c. daily, were administered to the entire body. About 150,000 units of vitamin A were administered daily. Salicylated creams were applied to the horny skin of the scalp, palms, and soles. Artificial sweating was induced by subcutaneous injections of pilocarpine hydrochloride at intervals of four to five days. Successive determinations of the courses of dark adaptation were made on various occasions during a period of 23 days. The values of the thresholds given in table 2 show a gradual return to normal levels while the patient was undergoing treatment. There is a decrease of from 0.5 log units (threefold) to about 1 log unit (tenfold) in the values of the threshold levels at various periods (minutes) of dark adaptation during the course of treatment.

TABLE 2

DARK ADAPTATION IN FOLLICULAR HYPERKERATOSIS

Values of the logarithm of the threshold levels (micromillilamberts) after various periods (minutes) of dark adaptation on days subsequent to treatment. Retinal stimulus area = $\frac{1}{3}$ degree. Light adaptation = 3 minutes to 160 foot-candles.

Time (minutes) Dark Adaptation	Days						Difference between Initial and Final Values (log unit)	Representative Normal Data (average 50 different determinations on 3 subjects)
	1	3	10	14	18	23		
I. Area 10 degrees above macula								
1	4.45	4.30	3.95	3.90	3.85	3.91	0.54	4.05
5	3.85	3.75	3.35	3.30	3.35	3.23	0.62	3.35
10	3.32	2.68	2.58	2.65	2.55	2.38	0.94	2.58
15	2.85	2.42	2.32	2.40	2.20	2.12	0.73	2.26
20	2.78	2.40	2.10	2.15	1.82	1.78	1.00	2.08
II. Macula								
0.5	4.92	4.75	4.55	4.75	4.31	4.28	0.64	4.15
5	4.15	3.90	3.63	3.68	3.35	3.41	0.74	3.42
10	4.10	3.90	3.60	3.70	3.42	3.35	0.75	3.34
15	3.95	3.88	3.65	3.68	3.43	3.40	0.55	3.25
20	4.05	3.75	3.53	3.68	3.50	3.32	0.73	3.20

COMMENT

During the course of our investigations there appeared in the literature two noteworthy contributions: one by Hecht and Mandelbaum[27, 28] and the other by Wald, Jeghers, and Arminio.[29] As we have stated, we were unable to discover any proof of vitamin-A deficiency in two subjects, during a period of six months or more on a very low vitamin-A diet (100 to 300 international units daily), as shown by photometric measurements of threshold values of the macula or of an area in the periphery of the retina. In contrast to our results, however, Hecht and Mandelbaum found that, in four normal subjects who were placed on a diet deficient in vitamin A, there were significant changes in the dark adaptations of both the rods and cones within two weeks of being placed on the deficient diet. In one case, after a month on the deficient diet, the threshold levels of the rods, after 30-minute dark-adaptation periods in each instance, had risen nearly 2 log units (one hundredfold) with an increase in the cone threshold of about 1 log unit (tenfold). The thresholds of all subjects tested by Hecht and Mandelbaum remained at abnormally high levels during a period of 30 days subsequent to the resumption of a normal diet supple-

mented with 50,000 units of vitamin A daily.

Moreover, in contrast to our inability to produce any significant changes (not in excess of 0.5 log unit) in the threshold levels, on the one hand, and, on the other hand, the relative ease of production of such changes, with difficulty of restoration, as found in the subjects examined by Hecht and Mandelbaum, a detailed study of one person by Wald, Jeghers, and Arminio showed definite changes in the levels of dark adaptation after he had been on the vitamin-A-deficient diet for four days and, after he had continued on the regimen for 25 days, subsequent ingestion of 100,000 units of vitamin A in the form of carotene in oil caused a restoration of the threshold to a normal level in 38 minutes.

Many questions are raised because of the definite differences in the results of the three groups of investigations. What are the normal requirements of the body and what is the minimal level of vitamin A? Are the apparently conflicting findings and conclusions of various investigators to be attributed to differences in amounts of vitamin A stored in the body or, more specifically, in the liver? Can the requisite delivery of vitamin A be furnished the retina in certain instances and at the expense of deposits of carotene and vitamin A in other parts of the body, such as the skin and fatty tissues? Some light has been thrown on these questions through the recent studies on vitamin A in the blood of normal adults by Steininger, Roberts, and Brenner.[30] The results of their investigations showed that the amount of vitamin A in the fasting blood is dependent on the amount in the diet. Although, as these authors point out, the evidence concerning the value of determinations of vitamin A in the body in judging the nutritional status is somewhat contradictory, the data show that consistently low blood values in the fasting state indicate the depleting of the body stores of vitamin A. On the other hand, high values of the vitamin A in blood show that the intake of this vitamin is adequate. Steininger, Roberts, and Brenner also showed that there is no correlation between the amount of vitamin A in the blood and the readings on the biophotometer. In three of the four subjects tested during a period of four months, the level of light thresholds remained practically constant and at normal values, irrespective of high or low levels of vitamin A in the blood.

These various investigations show that the rate of dark adaptation in persons whose rate is normal cannot be improved by daily supplements of vitamin A. Furthermore we believe there is little evidence to show that any considerable part of the population is suffering from a vitamin-A deficiency such as has been reported in the literature.

Conclusions

1. In three normal adult subjects, the thresholds of light brightness and the courses of dark adaptation of the macular areas and of regions 10 degrees above the macula were not affected significantly (less than 0.5 log unit) during the course of a dietary regimen very low in vitamin-A content (100 to 300 international units daily) for periods of 42, 160, and 190 days, respectively.

2. The experimental results were checked and corroborated by tests made with different intensities of, and exposures to, the light-adapting field (160 to 1,500 foot-candles) and with retinal stimulus areas of 0.33, 1, and 2 degrees, respectively. Other types of apparatus for the photometric measurement of visual adaptation gave comparable data.

3. These results show that, in certain normal adults, considerable periods of de-

ficiency in the intake of vitamin A may be maintained without producing any significant changes in rod or cone sensitivity.

4. Microscopic examinations of the skin of one of the subjects, who had been on a diet very low in content of vitamin A for 190 days, showed the presence of changes which, it is believed, generally occur in late stages of A avitaminosis. Restoration to a normal cutaneous condition, except for keratotic plugs in the hair follicles, occurred in about three weeks on normal diets supplemented with a fairly large (80,000 units) daily intake of vitamin A.

5. Measurements on dark adaptation have been made in a few clinical cases of persons reporting restricted and low vitamin diets for prolonged periods and in conditions of follicular hyperkeratosis. In general, in these conditions, threshold levels are above normal; high vitamin diets cause restoration to the normal range, although there are marked differences in the periods of time required.

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Discussion

Dr. Jonas S. Friedenwald: Dr. Joseph Mandelbaum asks this question:

"In view of the results obtained on a vitamin-A-deficiency diet by Jeghers, Wald, Adler, and McDonald, Booher and Callison, and Hecht and Mandelbaum—the last of whom have observed 17 cases—don't you think that these results are the exception rather than the rule? How do you explain this?"

Dr. Steffens: Of course it is possible that these results may be an exception that we are reporting. However, there were three of us on the same diet and all of us came from different sections of the nation. The "thresholds" remained at approximately the same level in each case during the period of dietary deficiency. We think that the discrepancy between the findings of various investigators may be explained by a variation in the ability of different persons to store vitamin A, although we have no experimental evidence to prove it.

Dr. Verhoeff: Dr. Arthur Alexander Knapp asks this question: "Since vitamin D_1 has been reported to be of value in dark adaptation, may I ask if you have any comparative results with vitamin A?

Dr. Steffens: No, Doctor, we haven't. During our period of dietary deficiency, each experimental subject had a daily intake of 15 drops of irradiated ergosterol. The consensus of opinion at that time was that our dietary requirement was very adequate in vitamin-D content and, therefore, we have no information to contribute to answer that question.

Dr. Edward Jackson: In recent articles in English literature, in London, there has been proposed that the light adaptation and dark adaptation should be taken as a test of vitamin-A sufficiency or insufficiency; but this applied to, and instances cited were entirely among, school children, generally of the early years of school life and in the strata of society where poor general nutrition was very likely to be. I would ask if you have made any investigation with refer-

ence to the liability of interference with light adaptation in children as compared with adults.

DR. STEFFENS: Yes, Dr. Jackson, that is being done now. Some work has been finished, but there is a group of doctors at the Mayo Clinic who has already examined a large number of children in the city of Rochester, Minnesota, and they have been unable to detect any evidence of vitamin-A deficiency in any of the children examined. An experimental diet is not being used in this investigation.

GLASS MEMBRANES IN THE EYE*

PART II. LAMINA VITREA CHORIOIDEAE

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The facts briefly mentioned here enable us to gain better knowledge of the fourth glass membrane of the eye—the lamina vitrea chorioideae. Like Bowman's membrane, Descement's membrance, and the lens capsule, it does not possess its own vessels nor (which is more important) its own cells with nuclei. It is dependent on the surrounding nourishing fluids and tissue. No cellular renovation is possible. We do not know anything about its metabolism nor about the deterioration which must occur in the performance of its important function.

This membrane is the first to show traces of *aging* at a time in which we believe that we cannot speak of senescence, as we will describe afterwards. The lens has an epithelium rich with cells growing out to form lens fibers, the waste products of its metabolism escaping through the capsule. The aging of the lens as an organ is shown by the limited production of cell material. The lamina vitrea chorioideae, without cellular material of its own, is bound to age like every colloidal membrane built once for all. Clinical and histological experience proves that the lamina shows degenerative changes long before any other organ of the body. Another regressive process—arcus lipoides corneae—starts very early also. Rohrschneider found, histologically, fatty infiltration of the corneal border in 9 out of 19 persons aged 21-30 years; that is, in 47.3 percent, and in 82.3 percent of persons from 51-60 years old. During the last month I have studied the fundi of all patients specially for the presence of the so-called colloid bodies or "Drusen" of the lamina vitrea chorioideae. I found these in nearly every patient over 30 years of age.

It is necessary to use the focused light of the electric ophthalmoscope (Friedenwald, Zamenhof), but it is seen quite well with the Keeler ophthalmoscope, also. The best result is obtained by changing from direct to indirect illumination in quick succession, as well as by changing from the convergent to the parallel beam. With the binocular Gullstrand ophthalmoscope, the tiny drusen are not easily recognized. Sometimes the pigment over the colloid body is not rarefied but denser, especially at its border. It is very easy to recognize the drusen when the pigment epithelium is lacking. They are best seen between the disc and the macular area.

* Part I appeared in the foregoing issue. In it Bowman's and Descemet's membranes and the lens capsule were described.

If attention has once been fixed on this point, it is hardly possible to find one normal person over 30 years of age without these drusen. Dark fundi are more favorable than fair ones. Histologically, these verrucae have been carefully described by H. Müller, who declared that they are to be found in the majority of eyes of adults, that after 45 years of age they are common, over 30 years of age they are not rare, and that they are even found in the eyes of some younger people. The first histological beginnings of the drusen are a kind of tiny drops and hyalin corpuscles in the lamina vitrea chorioideae (A. Meyer, Rosa Kirschbaumer, Salzmann, Schieck, Ginsberg).

If, clinically and histologically, we find these changes so early in eyes showing no other sign of alteration or aging, it must be assumed that they are preceded by physical and chemical modifications of the constitution of the lamina. This means that the membrane is already aging at a time when otherwise the patient would be said to be young. It is an early uncompensated process of decay.

If all the organs of the human body are so perfect, and fulfill their aims absolutely during the whole *average* lifetime, I would conclude, from the facts mentioned, that the biological expectation of life is shorter than the actual expectation resulting from the conditions of modern living. The average lifetime of the human being has been lengthened by civilization, but the constitution of the lamina vitrea chorioideae has not been influenced to the same degree.

By the aging of tissues is meant in the first place a biological cellular process closely connected with life itself. There is no doubt that continued cellular division without sexual impregnation necessarily induces cellular death. Besides this, the cellular complex of a mammalian, the domesticated mammalian, especially, and of the human being living in the most highly developed state of domestication, is exposed to a great number of noxae acting on certain tissues. We know that some food stuffs damage certain tissues—for example, cholesterin, the connective tissue of the cornea, uvea, and the vessel walls, and some drugs, such as dinitrophenol or galactose, the lens tissue. We do not know exactly where the limits of tolerance are. Yudkin has recently stressed that even the colloid bodies of the lamina vitrea chorioideae may be connected with a "stormy character of the early nutrition."

It is the task of medicine in the future to exclude these daily injuries, to protect these jeopardized tissues by fixing the amount of these substances that are dangerous when increased. We cannot eliminate the *innate factors* of the regressive metamorphoses, which are very often inherited. But it is not impossible to remove the *external* ones and to approach to the ideal—if it is one from the point of a general view—to the *physiological* cellular mortification.

We must suppose, therefore, that this colloidal membrane is in a stage of senile deterioration during the greater part of man's life, and it is to be expected that some of the many known but unexplained affections of the retina (the senile ones especially) are to be related to the regressive metamorphosis of this glass membrane.

The histological picture of the well-known "angioid streaks" is in some respects similar to that in senile changes (Verhoeff and Sisson, Hagedoorn). The latter stresses that in angioid streaks a specific regressive process of the elastic system occurs at a time when other cells and tissues of the body are still in good condition. New formation of elastic tissue is still possible, but evidently existing fibers do not reach the age of other tis-

sues. This means a precocious senility of the elastic fibers, a view supported by the fact that the degeneration occurs especially in regions in which the fibers are subject to continuous change in tension. It is possible that the mechanism which becomes defective in senility may become disturbed in an isolated specific tissue at an earlier age.

Fig. 7 (Loewenstein). Giant druse in a case of chorioretinitis.

In eyes with degenerative changes, with disturbance of their nourishment, as in chronic uveitis or detachment of the retina, the colloid bodies are markedly developed, sometimes to a grotesque size (fig. 7). We are not yet able to differentiate these "pathological" drusen from the "physiological" ones, except quantitatively. The process of "aging" is accelerated when the metabolism of the tissue demands an intensified current of nourishment (in the case of inflammation), or if the surrounding tissue produces an abnormal fluid (detachment of the retina).

The stream of nourishment starts from the choriocapillaris and passes through the lamina vitrea chorioideae, as especially Krückmann has confirmed, and we are convinced that it is essential for the deeper retinal layers. But it is not able to secure the function of the retina as we realize from the cases of embolism of the central retinal artery with intact choroidal-vessel system, which are not rare. Nevertheless, this current from the choriocapillaris, however, insufficient in itself, is essential for the retina, as we know from the cases of local sclerosis of the choroidal vessels, and from those with local inflammations limited to the choroidal tissue. The associated retinal area is nearly always functionally disturbed.

A direct purely mechanical local effect of the colloid bodies is assumed by Salzmann (1912) as well as by Krückmann (1906). Salzmann believes that the verrucae do not damage the function of the retina so long as they are not central. Without stressing it, Salzmann seems to assume that there must be some interference with the nourishment of the retina at the site of the drusen formation. It has very often been stated, that, in the drusen, cholesterin incrustations, colloid pearls, even lime deposits are not infrequently found; a fact which I can confirm, having studied many slides of such material.

It may be found in *frozen* sections that the lamina vitrea chorioideae is not cut in conformity with the other tissues. Sometimes a piece of this membrane is stretched over the neighboring tissue, highly refractile, completely transparent, and inclined to roll in. As may be well recognized with the stereoscopic microscope, it is *one* system. There is no difference between its anterior and posterior layers. The prominent free edge of the lamina is smooth, uncovered by any epithelium, and curls over and acts like a convex lens in front of the pigment corpuscles of the choroidal stroma. The impression that the consistency of this col-

loid membrane is very different from that of the neighboring tissue on both sides is thus produced by frozen sections of a certain thickness. The belief in a special function for this membrane is intensified by studying these.

The drusen are not equally stained. Commonly with eosin they stain pinkish turning red. Weigert and fat-staining are negative, but Rintelen (1939) several times noted positive fat reactions in cases of sclerotic vascular changes. I find it remarkable that, in the vast majority of these drusen which are situated on the lamina vitrea under the pigment epithelium, they rarely extend into the choroidal tissue (fig. 8). I could never detect, in these rare cases, a difference in the staining of the anterior and posterior drusen relatively to the position of the lamina

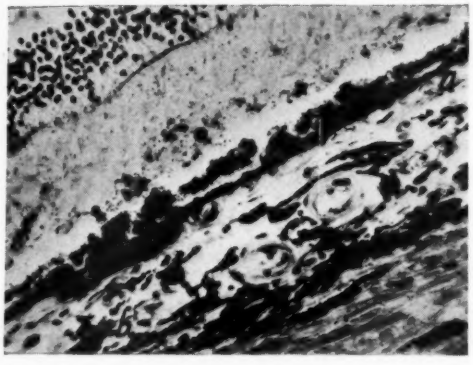

Fig. 8 (Loewenstein). Thickening of the lamina vitrea chorioideae in the anterior surface at (a), on the posterior surface at (b).

such as we found, for example, in the case of Groenouw's corneal degeneration in front of and behind Bowman's membrane. The drusen are eosino-acidophil.

We do not know the origin of these verrucae, but the assumption that they rise as a secretion of the pigment epithelium seems to me to be not very probable. In the first place, it would be a secretion against the stream of nourishment, and in the second, we find the biggest drusen very often in spots especially where the pigment epithelium is destroyed. I would suggest that it is a swelling of this colloid membrane, a senile dystrophy. Ginsberg shows a picture of a lamina vitrea chorioideae in a case of retinal detachment in which the glass membrane is thickened to a multiple of its volume.

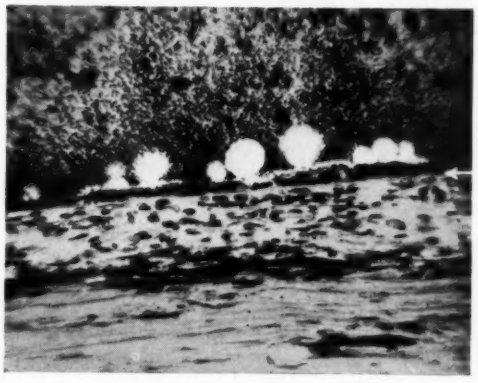

Fig. 9 (Loewenstein). Thickened part of the lamina vitrea chorioideae in the case of diabetic changes.

Local swelling under the influence of certain unknown fluids—abnormal local metabolism—produces such a reaction (fig. 9).

If my assumption is correct that the lamina vitrea chorioideae is primarily a selective filter, the early senile degeneration that is proved clinically and histologically must cause physiological senile changes beyond this membrane, as the conditions of permeation are changed. The findings of Reichling and Klemens, and of Reichling already described by Verhoeff, and quoted by Hagedoorn (I could not find the original paper), are a very interesting confirmation of this opinion.

There is a regular new-formed zone of connective tissue with vessels between the lamina vitrea chorioideae and the pigment epithelium in eyes of people

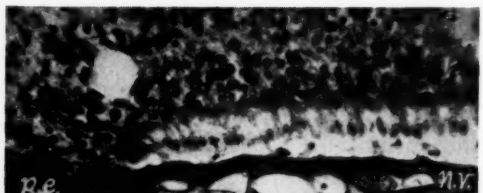

Fig. 10 (Loewenstein). Organized exudate between lamina vitrea chorioideae and pigment epithelium with new-formed vessels.

over 50 years of age (fig. 10). The lamina is irregularly thickened in wide areas in my different slides, the lumen of the vessels in these layers is open, the connective tissue rich with nuclei. The thickening of the lamina is not equally stained, but darker towards the choroid, and clearer to pink towards the pigment epithelium (fig. 11). Within the thickened lamina darker lumps stand out, not very sharply defined, and drusen are to be seen with their summits against the pigment epithelium (fig. 12). The big verrucae are often superposed not directly on the sharply defined lamina vitrea, but on a flat exudate of granular constitution (fig. 12). This exudate is commonly colorless, very extensive, and is formed also in spots without verrucae (fig. 13) where the pigment epithelium is lifted irregularly by the exudate. The lamina seems to be quite normal here as far as the histological slide is able to show (fig. 13). There it is possible to study the formation of the connective tissue between the lamina vitrea and the pigment epithelium (fig. 14). The exudate between the choroid and the lamina vitrea is covered (fig. 14) with pigmented choroidal tissue and the pigment epithelium is a broad layer. Half of this exudate—the anterior half only—is transformed into a young thin connective tissue with many young nuclei (fig. 14). I have found the lamina vitrea in senile eyes split into two layers, between them being young connective tissue. The senile change is well seen at the edge of the lamina where it terminates at the optic nerve (fig. 15), and at this point it is also thickened.

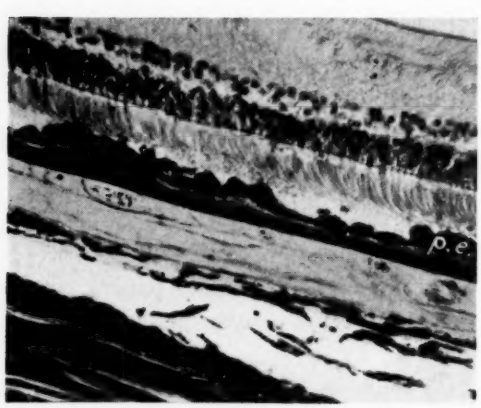

Fig. 11 (Loewenstein). Senile exudate between lamina vitrea chorioideae (greatly thickened) and pigmented epithelium.

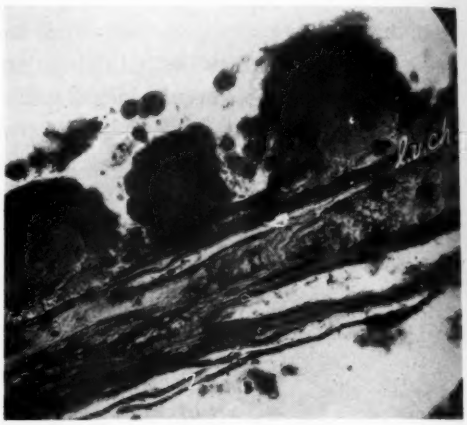

Fig. 12 (Loewenstein). Drusen with granulated exudate content. Senile degeneration.

Great masses of exudate, especially in detachment of the retina, show sometimes a continuity through a defect of the lamina vitrea chorioideae into the tissue of the choroid (fig. 16). There it is

very difficult to say whether the exudate invades the glass membrane from the retinal or from the choroidal side. We observe only one definite stage, without following out its development. But commonly there is little doubt about the genesis of this exudate, especially when the lamina vitrea as well as the pigment epithelium is preserved. The exudate is produced by the choriocapillaris, and permeates the lamina vitrea chorioideae—as the glass membrane has lost its closely

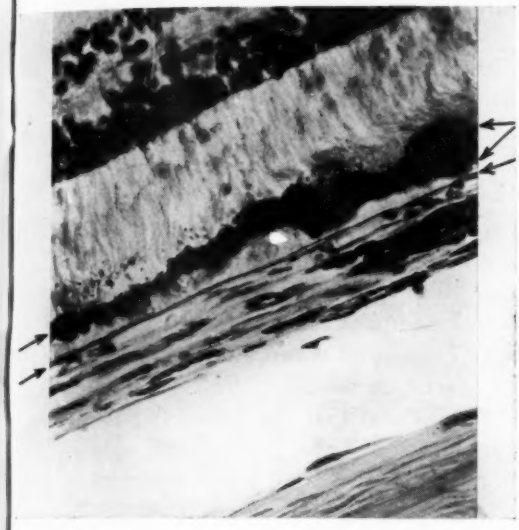

Fig. 13 (Loewenstein). Senile degeneration of the macula. Exudate between pigmented epithelium and lamina vitrea chorioideae (lower arrow).

delimiting power. Of course the theory that assumes a secretion from the pigment epithelium cannot be absolutely denied, but it seems to me to be improbable.

In senile and presenile eyes, an exudate arises between the lamina vitrea chorioideae and the pigment epithelium, changing into a young vascular connective tissue. The development of this new-formed layer varies greatly. In its higher degrees it often proceeds through the pigment epithelium, and produces there a new parallel subretinal mass, and may even reach into the retinal layer.

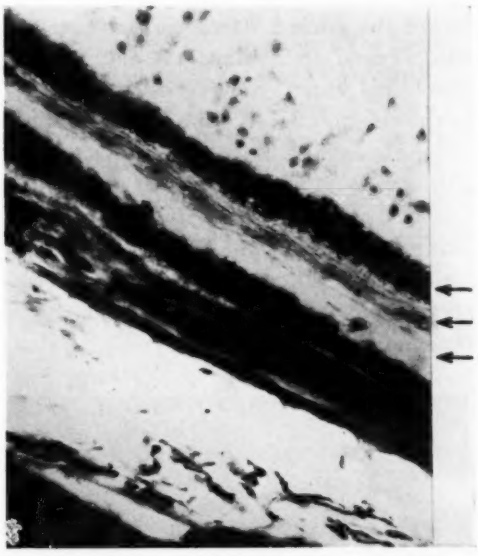

Fig. 14 (Loewenstein). Pigmented epithelium, upper arrow; new-formed connective tissue, middle arrow; exudate, lower arrow. The lamina vitrea chorioideae is covered.

Communications on the so-called senile "macular tumor" have been frequent since Elschnig published his carefully studied case. Both eyes show steadily growing macular foci, with prominence and decay of the function. Histologically Elschnig found a vascular connective tissue be-

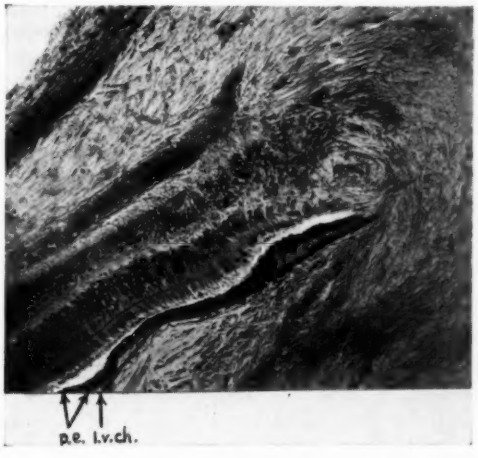

Fig. 15 (Loewenstein). Senile exudate at the optic-nerve border of the lamina vitrea chorioideae, between the lamina vitrea chorioideae and the pigmented epithelium (arrow).

tween the lamina vitrea chorioideae and the pigment epithelium. The lamina was absolutely intact, covered with verrucae, in the neighborhood of the "tumor" which Elschnig calls an inflammatory degenerative one. Wölfflin stressed that an *exudate* (as he believes through the gaps of the lamina vitrea chorioideae) causes chronic irritation of the retina. I was able to observe such an exudate in a slide of a senile macular tumor presented by Pro-

Fig. 16 (Loewenstein). Atrophia bulbi with detachment of the retina; retinal exudate in connection with chorioidea. Pigmented epithelium and lamina vitrea chorioideae locally destroyed. Big vacuoles over the epithelium-cell row. Arrow points to exudate passing the pigmented epithelium and lamina vitrea chorioideae.

fessor Brückner to Professor Ballantyne. In more highly developed cases, the tumor reaches throughout the whole retina as far as the nerve-fiber layer, and may be found at several independent parts of the retina, as in the case quoted.

Behr described such a case of senile macular tumorlike degeneration with an extensive exudate between the lamina vitrea chorioideae and the pigment epithelium, with a new-formed homogeneous connective tissue. It is his opinion that this new-formed connective tissue arises from a transformation of the pigment epithelial layer, and he already emphasized that *fluid,* rich with albumen, *passes through the degenerated lamina vitrea from the choriocapillaris.* He believes that the *primary phase* of the disclike senile retinal degeneration is a senile sclerosis of the *membrane of Bruch,* allowing a transudation from the choriocapillaris under the pigment epithelium, with secondary destruction of this layer.

Sandoz describes the slides of a senile bilateral macular tumor already briefly demonstrated by Vogt. The defects of the lamina vitrea chorioideae Sandoz observed in both eyes whereas Vogt had found the lamina intact in one eye. Both authors stress the opinion that the choriocapillaris plays the important role in cases of senile macular degeneration, while Rintelen emphasizes the uninterrupted series of his slides without finding a gap in the elastic membrane. Rintelen adheres to the opinion that the connective-tissue mass develops from the pigment epithelium. I feel that we must not underestimate the importance of the choriocapillaris even when we are not able to detect a defect of the lamina vitrea. What we find *microscopically* unchanged may not be normal *functionally.* We acknowledge of course a greater deviation from physiological metabolism of the retinal tissue if the living filter of the glass membrane is impaired, and that is not rare. Studying, for example, the anatomical reports of Rintelen, who investigated the eyes of people with arteriosclerosis, we are astonished how often the lamina vitrea chorioideae is described as being in a state of fatty degeneration. Rintelen stained these eyes, embedded in gelatin, with scarlet red. We see that there is a far-reaching chemical destruction of this glass membrane (not detected with

normal embedding and staining) which must influence its capacity for filtration as well as the composition of the permeating filtrate.

These senile macular processes are very common. I cannot understand why they have not been described before. The communications of the last few years about this clinical picture are not at all rare. I have observed several cases clinically. Nobody now, of course, would enucleate such an eye since we have recognized the nature of the change. *It is, as I believe, nothing else than the progression of a senile physiological development, starting very early, within the lamina vitrea chorioideae. The histological conformity with the typical senile degeneration is complete, verrucae, exudate, young vascular connective tissue between the lamina vitrea chorioideae and the pigment epithelium, between the pigment epithelium and the deepest layers of the retina and finally chronic inflammatory tissue within the retina. The whole histological development follows one line.*

For a long time the ophthalmoscopically striking changes in *myopia gravis* have been known. Investigating a high degree of myopia we find often the first pathological signs in the retinal center taking the form of fissures, the so-called "Lacksprünge" of Salzmann. Anatomically, tears in the lamina vitrea chorioideae are described by Salzmann and Behse. They are very irregular and notched. We observe several defects in the pigment epithelium (fig. 17) which I feel may not be artificial, but the defect includes a fissuring, not a crack in the pigment epithelium but a defect in the lamina vitrea chorioideae corresponding to the absence of the pigment epithelium. *There the filter of the lamina vitrea chorioideae is completely interrupted.* As commonly occurs when the pigment layer is disturbed, the pigment cells start moving to the retina and produce there the conglobate pigment-cell mass described by Förster-Fuchs. The tears within the lamina vitrea chorioideae and the pigment epithelium are probably sequels of bulbar expansion. The pigment spot is known, too, in cases of angioid streaks,

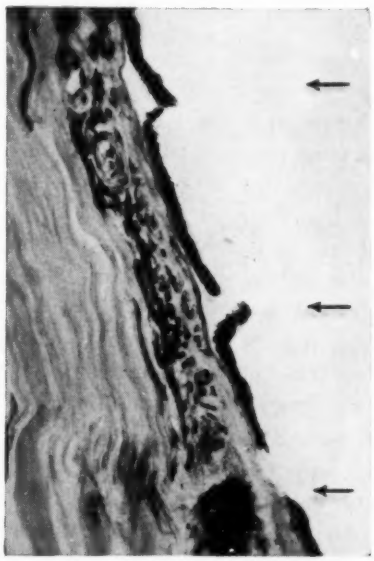

Fig. 17 (Loewenstein). Fracture of the pigmented epithelium; lamina vitrea chorioideae intact (artifact?), upper two arrows. Defect of the lamina vitrea chorioideae and pigmented-epithelium layer, lower arrow. High degree of myopia.

in which the importance of the breaks in the lamina vitrea chorioideae is acknowledged. They are comparable to tears in Descemet's membrane in cases of hydrophthalmus or of conical cornea.

It is of great interest to our question that defects in the lamina vitrea chorioideae cause a grave decline in the function of the eye at a very early stage. The undisturbed and exact filtration of this colloidal membrane in the macular area is essential for normal central vision. Even very small disturbances evoke degeneration and decay of this sensitive tissue in a very short time. In many cases of high myopia we

view with anxiety the rapid visual deterioration consequent upon the formation of these tears in the lamina vitrea.

The current of nourishing fluid is able, of course, to pass nearly unfiltered to the retinal tissue when defects of the lamina vitrea chorioideae break the continuity of the living filter.

We know very little about the role of the lamina vitrea in cases of *septic infiltration* of the choroid, and especially of the choriocapillaris. When we examine slides from cases of endophthalmitis septica, sometimes the impression is very strong that the separation built up by this membrane is nearly absolute. The retina and the corpus vitreum are filled with polynuclear leucocytes, and the choroid takes no part in the inflammation. Meller stresses this fact, and accepts the protecting function of the retina. But commonly we expect Bruch's membrane to behave in the opposite manner, for inflammation of the choroid causes a decrease of the filtering function of the limiting elastic membrane. According to Wessely, when we cauterize the sclera and produce an exudate of the choroid *progressing through the lamina vitrea chorioideae,* usually the retina becomes detached—very often not only partially. Commonly septic inflammation or traumatic infiltration of the choroid crosses the barrier of the lamina vitrea chorioideae at an early stage. In both cases—that of septic infiltration, as well as with heat application—we of course influence the chemical and physical constitution of this colloidal membrane and its permeability. Its most important function—the directed qualitative and quantitative filtration—becomes lost.

We may expect such changes of the lamina vitrea when it is degenerated, as in cases of *angioid streaks.* The retinal layers in front of the defects of the lamina degenerate as we know from clinical experience. The degeneration of Bruch's layer evidently allows an uncontrolled passage of fluid from the choriocapillaris, as Hagedoorn assumes as a result of his interesting histological findings in a case of angioid streaks. Exudate as a consequence of defects in the lamina vitrea in cases of angioid streaks is quoted in Boeck's paper.

In some senile eyes we find even an anatomical abnormality of the lamina of Bruch—swelling to several times the normal volume. It is easy to understand that such far-reaching changes influence the function of this organic filter. But for all the smaller variations, not detectable by our comparatively coarse histological methods, we are limited to suppositions based on physiological disturbances, and perhaps only to be detected by physical or chemical experiment. So we must collect carefully all clinical and anatomical data concerning this most important question, submitting them to the point of view under present consideration.

The glass membranes of the eye are *colloidal membranes*—flattened *gels,* subject like each colloid to *aging,* whether they are fluid or hard, thin (membranous) or in a thick layer, organic or inorganic, living or dead. This process is marked by *loss of water*—proved in many well-known experiments. "The water content of the human fetus is 94 percent, decreasing slowly to 67 percent in the adult," according to Marinescu, who calls natural death a "dehydration." With this dehydration the whole texture of the colloidal membrane is altered. It is unavoidable that microscopical fissures, cracks, and tears must occur. My view is that the permeability of this membrane must be changed in consequence—in a sense increased; while Jonas Friedenwald, opposing the details of my theory of cataract, assumes a decrease. His experiments with the lens capsule seem

really to prove a diminution of this important peculiarity.

The chief point of my assumption—a change of permeability in aging colloid membranes—seems to be established and a basis created for continuing the investigation in this direction. The rise of the vascularized connective tissue between the lamina vitrea chorioideae and the pigment epithelium is assumed in exactly the same way. In my opinion the glass membrane primarily is damaged by aging, loses its exact filtering power, and substances passing gather between the lamina vitrea chorioideae and the pigment epithelium. This exudate, with its content of albumen, provokes an irritation, with attraction of the vessels. Organization of the exudate arises with production of new-formed vessels containing connective tissue.

This biological reaction—the production of vessels and scars as a sequel to a regressive metamorphosis—is a *healing* one in other animal tissues. We do not acknowledge this effect in the glass membranes. Neither the pannus of the cornea nor the vascularized tissue of the lamina vitrea chorioideae mean an improvement of function due to the highly specialized development of this tissue. Quite the contrary. We find not too rarely that the growth of vessels between the avascular corneal tissue means an *irritation.* This is worth treating, as experience with different old cases of pannus (peritomy, cauterization of corneal vessels at the limbus) teaches. This reaction—the production of vessels—is not to be explained teleologically as useful—it is a biological one—sometimes exaggerated in its effect—an "error naturae."

Conclusions

It is a remarkable fact that in cases of familial corneal degeneration, the incrustations in all places where Bowman's membrane is preserved are divided into two different layers—the anterior frontal from Bowman's membrane is flat, acid-eosinophil, the posterior part basophil stained. From that observation the impression arose in the mind of the author that the function of Bowman's membrane must be that of a quantitative and qualitative filter, saving the most sensitive peculiarity of the protected tissues, the transparency of the cornea. While the other tissues have to be nourished only, and moderate differences in the chemistry of the nourishing fluids would not be of great importance, the transparent tissues demand the exact constitution of the nourishing fluid in osmotic pressure, pH, and special ions.

Histological studies show that the base of the foot-cells of the corneal epithelium is filled with unstained drops of different size, situated at the border line against Bowman's membrane. The drops are bigger in cases of high intraocular pressure. There the sharp border is blurred. Supravital staining of the human cornea shows that Bowman's membrane is stained with Giemsa grayish-pink, Descemet's membrane steel-blue. Especially supravital staining in bulk proves that Bowman's membrane holds back the Giemsa dye much more than does Descemet's membrane, the fiber layers of the cornea close to Bowman's membrane being stained slightly blue, while those close to Descemet's membrane are shining purple-red. The filtration of these two membranes is not only quantitatively but qualitatively different, Descemet's membrane allowing more Giemsa stain to percolate into the corneal tissue than does Bowman's membrane; the first containing more of the acid, the latter of the alkalin part of the stain.

The vesicles between the epithelial layer of the cornea and Bowman's membrane in cases of old glaucoma and acute

inflammation are explained as a retention of the lymphatic stream by the altered Bowman's membrane. If these vesicles with their débris are left for a longer time, they attract vessels, and a connective tissue arises, thus forming a degenerative pannus.

The lamina vitrea chorioideae is a glass membrane formed in the antenatal stage, its nourishment being controlled by the metabolism of its surrounding tissues. It shows signs of aging at a very early period (at 30 years very commonly), in the shape of verrucae. The author could find them clinically in nearly all patients over 30 years of age. Over 50 years of age the changes due to age are always present, a fact which is easily established clinically, with suitable ophthalmoscopic methods, and anatomically. We find regularly, on histological examination of the eyes of people over 50 years of age, a vascularized tissue (Reichling-Verhoeff) between the lamina vitrea chorioideae and its pigment epithelium. It is a kind of pannus degenerativus. The author advocates the opinion that the aging lamina vitrea chorioideae does not control the nourishing fluid flowing from the choriocapillaris to the retina as exactly as it should. An exudate is built between the lamina vitrea chorioideae and the pigment epithelium. This attracts vessels, and is transformed into a young connective tissue. The next stage of this aging degeneration is the splitting of the lamina vitrea and the developing of this vascularized connective tissue between the two layers. Not too rarely this connective tissue grows through the pigment epithelium under and in the retina, producing there tumorlike new growths (macular "tumors"). Defects of the lamina vitrea (and often of the pigment epithelium, too) can be easily demonstrated in cases of high myopia. Clinical experience shows that a short time after the appearance of the so-called "lack tears" (Lacksprünge) in the macular area, the function of the retinal center declines rapidly. The deficiency of the important controlled filtration within the most sensitive area of the retina is assumed to be responsible for the fast-progressing decay of function, very often combined with a luxuriant growth of pigment cells. In diabetic eyes I have been able to observe a thickening of Bruch's membrane. This change may have some bearing on the etiology of the white foci in the retina. Thermal and septic influences alter the filtrating membrane in such a way as to allow the passage of an unfiltered fluid into the retinal area, with its destructive results. In a case of endocrine cataract in a one-year-old child, the formation of a new subepithelial connective tissue within the exudate was discovered, and was explained in a similar manner.

The glass membranes as avascular colloidal tissue, fulfilling an important function, age much earlier than other tissues. Aging (histeresis) is a basic peculiarity of all colloids. Degeneration of the glass membranes is primarily the result of the physiological process of histeresis, but through other special influences, too (stretching through pathological growth, inflammation, systemic disease), their important function—the directed quantitative and qualitative filtration of the permeating fluids—may be destroyed. An exudate forms at the border of the glass membrane, very often with attraction of vessels, and there is new formation of young connective tissue—a degenerative pannus—a process well-known in the cornea, and also in the lamina vitrea chorioideae. A systemic disease of all glass membranes of the eye is unknown up to the present day.

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STANDARDS FOR OUTPATIENT OPHTHALMOLOGIC DEPARTMENTS*

II. Standards for nursing service
III. Standards for medical social service

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The idea of outlining standards for outpatient ophthalmologic departments was conceived in 1923 by a group of ophthalmologists in New York City, after a study of clinics in New York, Philadelphia, and Boston had been made. This group considered that standards for practice in eye clinics would be desirable. Therefore, the committee published standards[1] which seem to have played a part in improving conditions in eye hospitals and clinics in this and other countries. In the past, these standards have been useful not only in organizing eye clinics and departments but also in developing and evaluating the eye service in established institutions.

Because copies of the first studies were no longer available and since the practice of ophthalmology in clinics had changed, the Welfare Council of New York City, in coöperation with the National Society for the Prevention of Blindness, ophthalmologists, nurses, and medical social workers, undertook, through committees appointed for this purpose, to develop new standards. These threefold standards were approved by the New York Academy of Medicine, the Standards Committee of the North Atlantic District of the American Association of Medical Social Workers. They incorporate suggestions from the curriculum committee of the New York City League of Nursing Education. The New York State Department of Welfare and the National Society for the Prevention of Blindness recommend them as desirable.

All who took part in the preparation of the new standards realize that the varying conditions in clinics and localities necessitate certain differences in application. However, it is believed that the present recommendations will serve as a practical guide for those interested in improving outpatient ophthalmologic service.

The threefold standards are expected to be useful to deans of medical schools and hospital administrators as well as to specialists in the care of eye patients. They may be particularly valuable in focusing attention on a service which tends to be overlooked by the general administrators because a large majority of the patients are ambulatory and never have to be hospitalized. A great opportunity for prevention of blindness and conservation of eyesight is presented by these patients if the ophthalmologist is given full opportunity, through provision of the necessary equipment and skillful nursing and medical social work staffs, to carry through the treatment plans.

Since the medical standards have been published,[2] only the standards for nursing services and for medical social work are included in the present report.

II. Standards for nursing service

The nursing standards evolved are intended to cover a service that will not only care for eye patients, but may be used as a teaching unit in any nursing

* The preparation of this report has been aided by the Ophthalmological Foundation, Inc.

service allowing for undergraduate and graduate teaching.

ORGANIZATION OF THE NURSING SERVICE

The executive head of the nursing service may be the director of or professor in a school of nursing or superintendent of nurses, varying according to the organization of the nursing service in a particular institution. If a school of nursing is organized within the hospital or affiliated with the hospital, the director of the school is usually the executive head of the nursing service. In other medical institutions, the superintendent of nurses is usually the executive head of the nursing staff. Because of these differences the terms, director of, or professor in, a school of nursing *or* superintendent of nurses, are referred to in these standards as the executive head of the nursing school.

All connected with the nursing service are directly responsible to the executive head who has control of this branch of the service.

Supervisor, head nurse, general-duty nurses, nurse-technicians, and nursing aides are on an employment basis. Postgraduate and student nurses are appointed for educational purposes and should be so regarded.

Volunteer workers may be used if provision is made for ample instructions and supervision in the clinic.

1. Education

a. Nursing supervisor. Head nurse. The nursing supervisors and head nurses should be graduate registered nurses qualified by education to meet the membership requirements of the American Nurses Association and faculty requirements as established by recognized institutions. In addition they should have nursing experience in an ophthalmologic hospital or clinic, and should have a special interest in this field of medical practice and an understanding of the social implications of diseases of the eye acquired through an appropriate course of graduate study or through experience in a medical social service department of a hospital of approved standing with an ophthalmologic service.

b. General-duty nurse. The general-duty nurse should be a registered nurse. She should have a special interest in nursing in the field of ophthalmology and have shown a special aptitude for it. She should also be willing to spend adequate time in acquiring a scientific knowledge of diseases of the eye and their social implications.

c. Postgraduate nurse. The postgraduate nurse should be a registered nurse and a graduate from an approved school of nursing. She should be willing to spend sufficient time to qualify as a head nurse or nursing supervisor of an ophthalmologic service. She should be required to attend approved courses of lectures on diseases of the eye and their social implications, given in the hospital or in an affiliated institution of recognized standing.

d. Student nurse. The student nurse should be a member of an approved school of nursing. She should have completed her basic lectures and should have sufficient clinic experience to make possible her adjustment in a specialized field of nursing.

e. Nurse-technician. The nurse-technician should be a graduate registered nurse with special experience in an ophthalmologic hospital or clinic and have shown special aptitude for the detailed work of refraction and visual fields. She should have received special training under an ophthalmologist in vision, refraction, visual fields, orthoptics, and perimetry.

f. Nursing aide. The nursing aide should have a grammar-school education

and have sufficient ability to qualify her to do simple routine nursing duties under the teaching and supervision of the head nurse and to relieve graduate nurses of simple routine duties.

2. Selection

a. Nursing supervisor. Head nurse. Selection should be made by the director of the school of nursing or the superintendent of nurses.

b. General-duty nurse, postgraduate nurse, nurse-technician, and nursing aide. Selection should be made by the director of the school of nursing or the superintendent of nurses in consultation with the nursing supervisor and head nurse.

c. Student nurse. The selection of the student nurse should be made by the director of the school of nursing or the superintendent of nurses in consultation with the faculty member responsible for the assignment of clinic experience to student nurses.

3. Tenure

a. Nursing supervisor, head nurse, general-duty nurse, and nurse-technician. The term of service should depend upon the ability, efficiency, and adjustability of the individual. Preferably, a written statement of functions, duties, line of authority, salary consideration, and tenure should form the basis of employment. Termination of services should be by written notice given 30 days prior to date of leave or dismissal.

b. Postgraduate nurse. The term of service should be sufficiently long to enable a postgraduaate nurse to become thoroughly experienced in nursing practice and procedures in an ophthalmologic service.

c. Student nurse. The term of service should be from four to eight weeks, varying according to the policy of the school of nursing making the assignment.

d. Nursing aide. The term of service should depend upon her ability to perform the duties of nursing aide in a hospital, clinic, or medical institution where such services are in demand and her adjustment to this type of work.

4. Responsibility

All members of the nursing staff in the clinic should be responsible to the superintendent of nurses or the director of the school of nursing. In the efficient performance of their duties and assignments in the clinic they should be directly responsible to the nursing supervisor.

5. Duties

a. Nursing supervisor

Planning and direction of the teaching program for all nurses and others assisting in nursing functions.

Assisting the medical staff with the examination, care, and treatment of patients.

Adjusting problems relating to the nursing service brought to her by physicians.

Supervising and directing the work of the nurses assigned to the clinic.

Planning and supervising work of volunteers assigned to help nurses or physicians in the clinic.

Requisitioning supplies and instruments used in the clinic and being responsible for their proper care and safekeeping when not in use.

b. Head nurse

Responsible for carrying out that part of the teaching program as assigned by the supervisor.

Seeing that the policies and regulations of the nursing service are carried out efficiently in the clinic.

Assisting physicians with the examination, care, and treatment of patients.

Supervising and directing nursing personnel assigned to the clinic.

Assuming responsibility for the general upkeep of the clinic and for the care of clinical equipment.

c. General-duty nurse. Postgraduate nurse.

Assisting with the examination, care, and treatment of patients.

Carrying out instructions, routines, and duties assigned to her by the head nurse in the clinic.

Looking after supplies and clinical equipment.

d. Student nurse

Carrying out duties and routines assigned to her by the head nurse in the clinic.

e. Nurse-technician

Assisting the professional staff with the work of refractions, visual fields, orthoptics, and perimetry, for which she has been prepared by training and experience.

f. Nursing aide

Assisting the nursing staff with simple duties for which she has been prepared by teaching and practice.

III. Standards for Medical Social Work in Ophthalmologic Services

Services to patients are now carried out by personnel with several kinds of professional preparation, working together as a team. The composition of that team will vary with the nature of the group of patients to be diagnosed and treated. All the members must, however, be skillful each in his own special area and understand how to work flexibly with the other members of the team. In order to promote such quality of care for patients in ophthalmological services, a committee of the Welfare Council of New York City undertook the formulation of standards for medical social workers in these services. The committee was composed of medical social workers in hospital eye services and representatives from the National Society for the Prevention of Blindness and the New York State Department of Social Welfare, Division for the Blind.* The chairman of the Standards Committee of the North Atlantic District, American Association of Medical Social Workers, was called into consultation.

These medical-social-work standards are recommended for the present and should be considered with those developed for outpatient ophthalmologic clinics[2] and nursing† worked out by parallel committees of ophthalmologists and nurses. From time to time, as the general standards of the American College of Surgeons and the American Association of Medical Social Workers develop, it will be necessary to revise the specialized standards presented here. For the sake of clarity certain condensed phrases such as "basic professional education" and "medical social case work" have been used. Amplification of these phrases will be found in the literature of the field and the reports of special committees.

As the number of medical social workers with modern professional education increases, administrators will find it easier to obtain the kind of worker recommended here. An advanced course offered at Washington University, Saint Louis, is at present the only opportunity for special preparation of medical social workers for eye services.

Organization of Medical Social Service

A medical social service department is an integral part of a hospital or out-patient department and hence a close administrative relationship should exist between it and all other departments within

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* Chairmanship of the committee was held successively by Ruth McCoy, Jeanne Wertheimer, Grace Cooke, Eleanor Brown Merrill.

† Committee on Nursing Standards, Ruth C. Williams, chairman.

the institution. Conferences should be held at regular intervals with the medical and nursing staff and the superintendent of the institution to discuss policies and problems and to evaluate the medical social work done in the clinics.

The director of the social service department should be a person of executive experience and ability, and should be qualified by professional education and training to meet the requirements for active membership in the American Assocation of Medical Social Workers, and should be a participating member of the district organization.

The selection of the director of medical social service should be made by the superintendent of the hospital or outpatient department with the approval of the board of trustees.

As a member of the medical team and as a representative of the hospital administration and of the community, the eye medical social worker, with her knowledge of eye diseases and their social implications, has an important role in the conservation of vision and the prevention of blindness. Through processes of medical social case work she may bring to the physician social, environmental, and emotional factors in the life of the patient which may be of assistance to him in making a medical diagnosis. At the same time she stimulates in the patient a self-reliance and readiness to think through his own problems.

1. Education and Training

Eye medical social workers share with other medical social workers the need for basic professional education and training. They should be qualified for active membership in the American Association of Medical Social Workers. Before entering the specialized service it is expected that, in addition, they should have availed themselves of opportunities for special eye training through supervised experience, or in such courses as are approved by the professional organizations.

2. Selection

Selection of the chief medical social eye worker and staff medical social eye workers should be made upon recommendation of the director of the social service department with the approval of the superintendent and the chief of the ophthalmological service.

3. Duties

a. Chief medical social eye worker. The chief medical social eye worker should be responsible for supervision of the staff medical social eye workers and for seeing that the policies of the clinic and medical social service department are carried out efficiently. Among other methods of promoting staff efficiency, the holding of staff meetings at least once a month is highly recommended.

b. Staff medical social eye worker. The staff medical social eye worker should be responsible for interviewing patients in the clinic and for doing medical social case work in accordance with the practices and procedures of the medical social service department.

4. Staff

a. Number of staff. The number of staff members required is determined by the clinic registration, the number of sessions held each week, and the policies of the whole institution. Due consideration should be given to such studies as may be helpful in determining a proper case load.

b. Clerical assistants. An adequate number of trained clerical workers for keeping records and statistics and for other clerical routine should be made available. The number needed will vary according to the size of the clinic and established practices in regard to record keeping and clerical routine. At least one clerical

worker should be available for every three staff workers.

5. Volunteers

The use of volunteers in a clinic, and their duties and assignments, should be determined by the director of the medical social service department in conference with the chief medical social eye worker, chief of the ophthalmological service, and hospital superintendent. The following points are suggested, however, as helpful in the planning and guidance of a volunteer program:

a. Volunteers should be required to submit written application with outline of experience.
b. Written instructions as to regulations and practices of the clinic with statement of duties and responsibilities should be available to each applicant.
c. Direction and supervision of volunteers in the clinic should be the responsibility of the staff social workers to whom they are assigned.
d. Individual conferences with volunteers should be held as frequently as circumstances warrant.
e. Volunteers should be stimulated to increase their knowledge and usefulness in the clinic by attendance at lectures, selected courses, and such hospital conferences as might be of interest and value to them.

Summary and conclusion

In this presentation of nursing and medical social service standards for eye clinics, standards are recommended for consideration in the establishment of eye clinics and departments. They should also aid in reorganizing present eye services.

The committee is confident that the intelligent application of these standards will aid in preventing unnecessary blindness.

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THE EVOLUTION OF LENS LESIONS IN EYE PERFORATIONS AND RUPTURES

A MEDICO-LEGAL STUDY

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In a previous survey of 55 lens lesions in eye contusions[1] an attempt was made, in the light of the biomicroscopic contributions to the subject by Vogt, to clarify some obscure points in the diagnosis, in the determination of age, and in the prognosis of the lens lesions observed in eye contusions.

That survey tended to confirm the specific morphology of the lens lesions resulting from contusions as resting on: (1) subcapsular beginnings, (2) tendency to equatorial and posterior subcapsular involvement, and (3) on regional segmentlike localization. It also defined the quite characteristic varieties of the juvenile and of the adult contusion lens lesions. It called attention to some of the medico-legal problems in causal relation involved, particularly in the less-well-defined senile contusion lens opacities. It pointed out that in spite of the well-established "remotio cataractae traumaticae" phenomenon of Vogt it cannot be utilized, without reservations, in determining the age of a lens opacity for medico-legal purposes, because of a too widely varying rate of recession into depth, depending on other factors besides its age. As a result we find: (1) that while a deep opacity argues for age, a superficial opacity need not be recent; (2) that the density of an opacity resulting from compression is an additional clue to its age; (3) that coronary and lamellar opacities as well as the activation of senile opacities may be the result of contusions; (4) that neither anterior- posterior- nor equatorial-capsule ruptures are demonstrable in them; and (5) that the prognosis should be guarded in contusion lens lesions after the age of 30 years. It also suggested restriction of the term "cataract" to complete lens opacification and that mere opacities should not be called cataracts.

The present survey of lens lesions, observed in the course of the same period in the examination of cases of eye perforations and ruptures, in which lens penetration to a certain depth or its double perforation and a possibly transient or persistent hypotony were additional complicating factors—possibly affecting the "remotio cataractae traumaticae" rate—throws additional light on some of the problems dealt with.

The immediate or retrospective diagnosis of a recent eye perforation or rupture presents little difficulty, and the medico-legal problems arising in connection with them, compared with those in contusions, are correspondingly easier to solve. In spite of this, however, there are encountered in the examination of eyes for workmen's compensation, too many overlooked intraocular foreign bodies; many eye perforations and ruptures, too, are undiagnosed, often having been regarded as merely corneal abrasions or opacities or conjunctival lacerations. It is quite true that conjunctival hemorrhages and lacerations may easily hide a limbic or scleral perforation, with or without the retention of a foreign body. Difficulties present themselves in the retrospective diagnosis of older perforations. Very old corneal perforations are not always recognizable as such. Biomicroscopic demonstration of conjunctivo-scleral adhesions

which prevent the conjunctiva from gliding freely over the sclera, of subconjunctival foreign bodies, of conjunctival scars, and linear pigmented scleral ruptures, is often very helpful, particularly when opposite a chorioretinal scar in the fundus. Yellowish nodular capsular epithelial proliferations have also been found helpful in the diagnosis of a late siderotic cataract, after the fading-out of a true siderosis lentis following the extraction of an intraocular foreign body many years previously.

This survey, however, is primarily concerned with the problems of the specific morphology, of the determination of the age of a lens opacity, and of its prognosis; that is, with the life history of lens lesions from mechanical injury.

The evolution of a lenticular opacity from perforation or penetration of the lens is, according to Fuchs,[2] as follows:

"All injuries which make an opening in the lens capsule result in opacity of the lens. . . . In traumatic cataract it is the rule that the opacity of the lens becomes total. . . . Exceptionally, however, cases are observed in which the opacity of the lens remains partial or indeed actually disappears again. For this to occur, the capsule wound must be very small, so that it closes quickly and the aqueous has no longer access to the lens fibers. Most favorably situated in this regard are those capsular wounds that lie behind the iris, by the adhesion of which to the wound the latter is very soon closed up. In such cases it may happen that a circumscribed opacity remains confined to the site of injury, or, if a foreign body has penetrated the lens, is found only along the track of the wound. By resorption of the opaque portions the opacity itself may even in part clear up again. . . ."

Wagenmann[3] quotes Leber and Schirmer to the effect that capsule scars are formed by epithelial proliferations, and P. Knapp to the effect that posterior-capsule ruptures are repaired by epithelium from the lens equator, and that opacification of the human lens with a ruptured capsule proceeds much more rapidly than in the case of the rabbit, in which even large capsule ruptures are quickly sealed by a fibrin deposit. Wagenmann believes that there is an early passage of fluid from the anterior part of the lens across the equator to the posterior portion, that posterior cortical stellate or disc-shaped opacities are due to injuries near the equator, and that posterior-capsule ruptures are rare in man. He also calls attention to the fact that lenses with partial opacities are less resistant to further injury or disease and may become total cataracts after the lapse of many years, that nuclear and lamellalike opacities are sometimes observed as special forms of partial traumatic opacities, particularly in the young and after discissions. These phenomena are also observed experimentally in the rabbit. He observes, moreover, that lens absorption may cause its flattening and increase of hyperopia.

Allport,[4] on the other hand, believes that in traumatic-cataract cases the posterior capsule and the hyaloid membrane are frequently ruptured.

Levy[5] reports an increase of 4.75 diopters of hyperopia, following a capsule injury.

The 62 cases of lens lesions in eye perforations and ruptures reviewed here were all observed in the course of the years 1938 and 1939, the same period covered by the contusion opacities studied. Only those with periods of observation of over six months were utilized and therefore cases of injuries occurring in the latter half of 1939 are not included. Some cases are as old as 25 years. Cases severe enough to produce immediate "traumatic cataract," or to lead to enucleations, or those presenting aphakia when first seen (these constitute approximately a number equal to that reiewed for the period) were not dealt with. A few cases of eye perforations without lens lesions or with only epicapsular anterior or posterior deposits or with incomplete data were left out.

For the purpose of greater clarity in the analysis, the cases in which there was retention of an intraocular foreign body are grouped separately from those in which retention did not occur. In both, the order observed in the tabulation has been that of the persons' ages when last examined and the suborder that of the ages of the lens opacities. The "end result" column and the illustrations embody the writer's observations and sketches made at each examination.

The large number of cases in which definite injuries to the lens capsule were observed which gave rise to partial opacities only would seem not to bear out the quoted statement from Fuchs to the effect that they are exceptional. In addition, the favorable outcome of eye perforations and ruptures in about one half of the cases for the period covered contrasts markedly with Medwedjew's[6] report (1930) that useful vision was retained in cases of ocular perforations in only 15 percent, in Soviet Russia. It should be borne in mind, however, that this was the period of rapid industrialization of an industrially untrained population and may not be the case at present.

As has been noted in the case of the survey of contusions, medical attention in metropolitan New York is prompt, and attention is secured in 80 percent of the cases on the same day or immediately; in 90 percent, within 24 hours. This, of course, makes for early available medical data and, in addition, argues for pain as a more or less constant phenomenon of some significance in the critical analysis of medico-legal cases.

Lens lesions in cases of intraocular foreign body

Sena[7] reports for the Argentine that perforating injuries constitute 5 percent of all ocular injuries and that intraocular foreign bodies constitute 1 percent of such injuries, four fifths of the latter the result of industrial accidents. The left eye is said to be more often affected. Sixty percent of intraocular foreign bodies are reported to be iron particles, and 75 percent of these weigh less than 20 mg., some running as small as 1 mg. in weight. Eighty-two percent are said to find their way to the posterior segment, including the ciliary body, and only 18 percent to remain in the iris, anterior chamber, or lens. They pass via the cornea in 72 percent of cases. He states that he has observed a double perforation in hunting accidents only, not in industrial accidents. Twenty percent only were in the upper hemisphere, and then were always incarcerated in the sclera.

Begle[8] finds that small fragments do not evacuate the anterior chamber and when they perforate the cornea near the limbus pass through the zonule, leaving the lens uninjured in 9 cases out of 10; that in passing obliquely they may cut the iris near the peripheral margin and still leave the lens uninjured. He also finds that fragments of less than 5 mg. weight may become entirely oxidized and need not show in the X-ray film. Fragments, when traversing the lens, generally leave only anterior- and posterior-capsule opacities, punctate anteriorly, and disc shaped posteriorly, in 7 cases out of 14. He reports three cases of intralenticular foreign-body extractions in which the lenses remained clear, and one case of migration of a foreign body in the lens believed due to the patient's having come into a magnetic field in the factory.

Michail[9] reports three cases of contusion opacities of the lens produced by foreign bodies sliding tangentially on the lens surface.

Meesmann[10] reports the observation of rare lens opacities near the posterior cap-

sule at a distance from the point of exit of a foreign body which traversed the lens.

According to Wagenmann, *loc. cit.*, passage of a foreign body through the lens often leaves only capsule scars and a track but no opacity.

In regard to the tolerance of the lens for foreign bodies, Fuchs, *loc. cit.*, says: "The lens, on the contrary, possibly on account of the sluggishness of its tissue metamorphosis, is the part of the eye in which foreign bodies are relatively the best borne" (p. 817).

Blatt[11] also finds foreign bodies in the lens well tolerated and believes they may be let alone.

Amman,[12] on the other hand, on the basis of his own experience, has arrived at the conclusion that intralenticular particles of iron, because of their toxicity, should be removed as advised by Elschnig.

In regard to the anamnesis and the dependability of X-ray studies, Allport, *loc. cit.*, says: "I find that patients are not trustworthy witnesses under these conditions (that is as to the presence of an intraocular foreign body). Most men who have received injuries assert that there is nothing inside of the eye, but I pay no attention whatsoever to opinions of this kind. I must have good X-ray pictures. Not all X-ray pictures are reliable. I have been deceived both ways."

Sherman [13] reports 11 out of 95 intraocular foreign bodies undiscovered by X ray and one misleading as to localization. In 25 percent of cases ophthalmoscopy has been found sufficient for diagnosis and localization; extraction successful in 50 percent of cases without the aid of X-ray localization.

Kiehle[14] deplores the lack of reports covering long periods of observation of intraocular-foreign-body cases and suggests that: "Peace-time organizations at all comparable in authority with the military are the various state industrial accident commissions and of course most of these accidents occur in industry. At least, as long as interval payments in compensation are made, the commissions retain a definite authority over patients and can require the remaking of visual tests at regular intervals. A very real contribution to the subject could in time thus be obtained by careful and continued rechecks at six months intervals. The present rule in the settlement of these cases by insurance companies and by state accident commissions is to wait not longer than six months before determining the permanent partial disability. A much closer conjecture can be made after two years have elapsed."

The practice in New York state is to keep these cases under observation much longer, as long as three years, except in cases of obviously permanent industrial blindness, and the facilities for reopening cases are so generous that this series includes cases as old as 25 years.

An analysis of the intraocular-foreign-body cases, condensed in table 1, brings out the following pertinent facts:

The age distribution is approximately that for the industrial population in general; namely, twice as many workers under 40 years are represented. Eighteen right eyes and 15 left eyes are involved.

Eighty percent of the foreign bodies perforate the cornea. The extractions are mainly by the anterior route. Two double globe perforations are represented by cases 8 and 23. A doubtful one is case 27. Iris perforations are noted in 60 percent of them, but there is only one record of observations of hyphemia in the attending ophthalmologists' report.

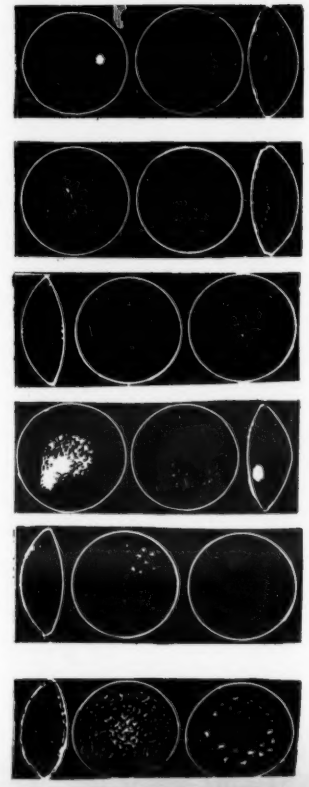
In spite of the high incidence of entry of foreign body via the cornea, only 6

TABLE 1

LENS LESIONS IN CASES OF INTRAOCULAR FOREIGN BODY

Number Name Age	Date and Nature of Accident	Date of First Medical Attention. Nature of Injury	Period of Observation	End Results		
				Eye, Vision	Cornea, Sclera, Pupil, Iris, Vitreous, Fundus and Other Data	Lens Findings
1 W.A. 21	12/14/38 While hammering struck eye	Same day by gen. prac. f.b. removed from cornea. 6 mos. later ophth. diagnosed intraocular f.b. below in vitreous, but in view of 20/20 vision let it alone	1 year	O.D. L.P.	Cornea, iris, and lens-capsule perforation at "9 o'clock"	Capsule opacity at 3 o'clock and siderosis 9 months after accident, with complete opacification
2 K.Ch. 24	12/10/37 Eye struck while driving	Same day. Scleral laceration. Intraorbital f.b. by X ray. F.b. retained	2 years	O.D. L.P.	Perforation of nasal sclera over ora. F.b. visible, 2-disc diameters nasally from papilla	Siderosis lentis noted as reported on 18th day. Marked siderosis with yellowish outstanding fetal suture with bifurcation of stem below. Later posterior subcapsular opacification
3 M.M. 29	8/1/38 Struck by brush wire	Same day. One-inch-long wire broke in attempt at removal from cornea. Fragment extracted	1½ years	O.S. 20/20	Nasal keratome incision. Iris root perforation at "9 o'clock" and iris atrophy halfway to border. No vitreous pigment. Fundus normal	Anterior subcapsular axial opacity. Later feint posterior subcapsular axial opacities and diffuse anterior scattered equatorial opacities
4 W.H. 29	10/1/34 Distilling flask exploded during experiment	Same day. Numerous glass particles in both globes. O.S. enucleated 6 weeks later	5 years	O.D. 20/40	Cornea and bulbar conjunctiva studded with glass particles. Two cystoid cicatrices lower temporally with posterior synechiae	Lower temporal glass particle (?) in lens covered by hazy overlying cortex and capsule opacity. Posterior capsular ground-glass appearance
5 R.F. 30	3/9/38 Struck while tightening bolt	Same day. Intraocular f.b. Extraction not successful	2 years	O.S. 20/20	Lower nasal scleral scar. F.b. in lower nasal fundus bounded by choroidal atrophy. Retinitis proliferans	Occasional small upper temporal posterior subcapsular opacities, and epicapsular diffuse greyish deposits, posteriorly
6 S.Ch. 30	8/13/34 Struck by tack	Same day. Laceration of cornea	5 years	O.S. L.P.	Cornea-iris perforation at "5 o'clock." Vision remained at 20/20 for 3 years. Vitreous opacities appeared and increased. Retinitis proliferans appeared at site of lower-temporal-fundus lesion. Finally hypertension and cupping. X ray persistently negative	Siderosis lentis first noted 7 months later. Posterior subcapsular iridescence 3 years afterwards. Recession of siderosis to disjunction band in 5 years only

O.D.← Anterior Posterior Section
O.S. →Section Posterior Anterior



7 M.V. 31	11/10/38 Struck by sliver off bullpoint	Same day. In spite of negative X ray, f.b. suspected and extracted	1 year	O.D. 20/25	Central corneal perforation scar. Upper temporal iris coloboma	Anterior and posterior axial-capsule opacities with track connecting them. Recession to disjunction band in 14 months. Temporal posterior epicapsular pigment
8 D.H. 31	10/7/38 Struck while hammering	Same day. Perforation of cornea and sclera. Intraocular hemorrhage. F.b. in orbit	1 year	O.D. 20/20	Scar at "3 o'clock" at limbus. Anterior synechiae. Meridional choroidal atrophic streak below, running close to disc. Double perforation	Anterior temporal epicapsular pigmented opacities and subcapsular equatorial anteroposterior opacities
9 L.S. 31	8/6/36 Struck while heating goose-neck	Same day. Hyphemia. F.b. diagnosed and removed only 13 months later	3 years	O.D. L.P.	Upper temporal scleral scar close to limbus	Siderosis noted in one year, with subcapsular posterior opacification. Complete opacification 3 years afterwards, with large siderotic patches recessed into cortex and water clefts running into them
10 L.J. 32	9/1/37 Struck by particle off driving shaft	Same day. Intraocular f.b. in iris, extracted. Vitreous hemorrhage very slow in absorbing	2 years	O.D. 20/25	Corneal perforation scar and iridectomy coloboma below	Anterior and posterior epicapsular pigment below. Anterior subcapsular lens opacity nasally and anterior subcapsular punctate scattered opacities at level of disjunction band below
11 Z.P. 32	2/2/37 Struck in explosion	Same day. Intraocular f.b. Extraction not successful	3 years	O.S. 20/100	Lower temporal scleral perforation. F.b. above macula	Posterior polar-lens opacification noted in 5th month. Macular star in 17 months, with greenish discoloration of Descemet's membrane, iris, anterior-lens capsule and very vivid vitreous framework. Chalcosis bulbi
12 L.H. 33	8/23/38 Struck while hammering	Same day. Corneal abrasion. Intraocular f.b. diagnosed 1 month later and extracted by posterior route	1 year	O.D. 20/25	Cornea-iris perforation at "3 o'clock." Vitreous opacities. Lower temporal chorioretinal atrophic patch	Equatorial anteroposterior opacity at "3 o'clock" with extension up and down
13 A.E.B. 35	8/5/38 Struck while grinding	3d day. Intraocular f.b., extracted	1 year	O.D. 20/20	Cornea-iris perforation at "5 o'clock." Iris-root transillumination at 10. Vitreous opacities. Upper temporal peripheral chorioretinal scar	Anterior upper temporal subcapsular and lower nasal anteroposterior subcapsular opacities
14 M.J. 35	10/4/30 Struck while cutting bolt	Same day. Intraocular f.b. back of lens, extracted 8 days later	9 years	O.D. 20/200	Cornea-iris perforation at "2 o'clock." Lower nasal anterior synechiae and iris depigmentation. 20/20 vision retained for 8 years, when hypertension and cupping noted (following electric burn of right side of face)	Anteroposterior lower nasal subcapsular opacity with recession in 9 years to disjunction band only

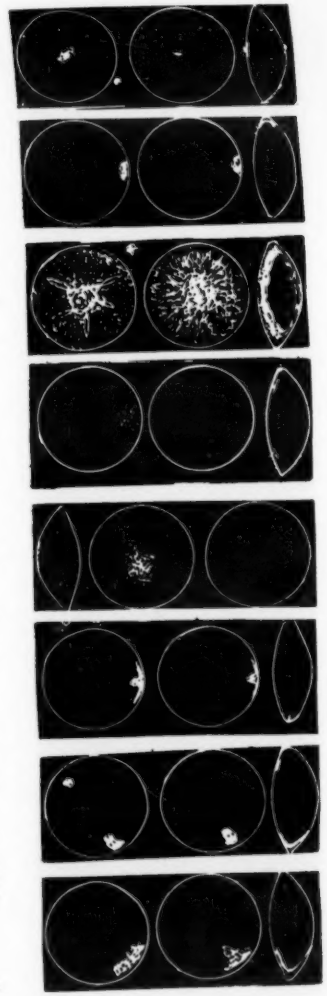
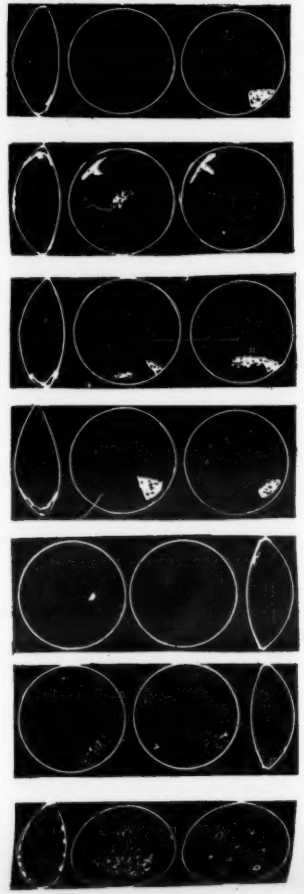


TABLE 1 (*Continued*)

Number Name Age	Date and Nature of Accident	Date of First Medical Attention. Nature of Injury	Period of Observation	End Results		
				Eye Vision	Cornea, Sclera, Pupil, Iris, Vitreous, Fundus and Other Data	Lens Findings
15 G.M. 36	11/5/38 Struck while hammering	3d day. Intraocular f.b. extracted	1 year	O.S. 20/20	Scar at limbus and anterior synechiae at "3 o'clock"	Anterior subcapsular opacity at "5 o'clock"
16 McL.K.J. 37	10/19/38 Struck by piece of cold chisel	Same day. Intraocular f.b., removed next day	1 year	O.S. 20/25	Cornea-iris perforation upper nasally. Site of f.b. marked by scar near disc nasally and extraction path by choroidal atrophic streak. Macula folds	Equatorial anteroposterior subcapsular linear upper nasal opacity with an extension up and down and greyish rosette-shaped posterior subcapsular axial opacity
17 M.Th.	9/12/38 Struck while using air machine	Same day. Intraocular f.b., extracted 11 days later from vitreous	1 year	O.S. 20/100	Lower nasal corneal perforation. Iris coloboma-lower temporally. Anterior and posterior synechiae	Lower temporal anterior massive and scattered posterior epicapsular pigment. Anteroposterior lower temporal subcapsular opacities
18 S.A. 37	2/28/37 Struck while coupling steam hose	Second day. Intraocular f.b., extracted	3 years	O.S. 20/20	Cornea-iris perforation lower temporally. Proliferating retinitis. Site of f.b. near disc	Anteroposterior lower temporal subcapsular opacities, posterior wedge-shaped with iridescent tip
19 L.A.F. 37	6/19/39 Struck while hammering	Next day. F.b. extracted from lens a few days later	½ year	O.D. 20/25	Upper temporal keratome scar incision. Central corneal perforation	Capsule perforation at "3 o'clock," recession to disjunction band in 6 months. Punctate opacities reaching adult nucleus back of recession
20 M.J. 38	2/25/38 Struck while at work	Same day. Intraocular f.b. extracted 4 days later	2 years	O.D. L.P.	Lower nasal corneal perforation and coloboma	Anterior and posterior subcapsular opacities and track running obliquely from anterior nasal to posterior temporal lens
21 T.E.F. 38	3/10/37 Struck in removing barrel hoop	Same day. First aid by layman. Six weeks later, because of pain, intraocular f.b. diagnosed and extracted posteriorly. 3 months later detachment and operation for it	2 years	O.S. 20/60 metamorphopsia	Lower nasal scleral perforation and chorioretinal scar. Vitreous opacities	Opacities noted soon after detachment operation in form of large anterior subcapsular vacuoles and posterior diffusely scattered opacities

O.D.←Anterior Posterior Section
O.S.→Section Posterior Anterior



22 M.F.A. 39	1926 No data	Intraocular f.b., extracted 2 years after accident	11 years	O.S. 20/200	Faint scleral scar below	Anterior capsule fold at "8 o'clock," scattered subcapsular nodular masses with faint suggestion of siderosis, deep anterior cortical opacities and posterior subcapsular iridescence
23 Z.W. 41	5/13/36 Struck while pulling gear	Same day. Double perforation diagnosed, and X-ray localization back of globe	3½ years	O.D. 20/40 ?	Cornea-iris. Perforation at "2 o'clock" outside limbus. New X ray localizes f.b. at equator outside globe. Small round chorioretinal scar at "7 o'clock" suggestive of exit	Anterior capsular opacity at "2 o'clock" and two posterior capsular opacities at "2 and 3 o'clock," latter one below the other, connected by track?
24 T.A. 43	10/24/38 Struck while hammering	Next day. Intraocular f.b., extracted. 2 months later intraocular hemorrhage	1 year	O.D. L.P.	Lower nasal scleral entry perforation and lower temporal exit perforation. Lower nasal fundus scar and retinitis proliferans lower temporally. Vitreous blood	Smooth homogeneous disc-shaped posterior opacity at level of disjunction band
25 P.S.S. 43	7/5/35 Struck while hammering	Same day. Intraocular f.b., in posterior lens protruding into vitreous, extracted	4 years	O.D. 20/40	Upper nasal and lower nasal perforation scars. Iris hole lower nasally. Lower nasal large choroidal atrophy in fundus	Capsule opacity upper nasally. Recession to disjunction band only in four years. Track through lens. Lower nasal subcapsular opacity anteriorly and larger one posteriorly and cortical
26 A.J.H. 44	7/27/38 Struck by piece off chisel	Same day. Intraocular f.b., extracted	1½ years	O.S. 20/20	Limbus perforation at "11 o'clock" and iris root perforation at "11 o'clock." Keratome incision at "10 o'clock." Vitreous pigment	Upper nasal anterior and posterior epicapsular pigment with subcapsular small opacity opposite latter
27 B.L. 44	9/28/37 Struck while hammering	12 days later. Laceration of cornea. X ray negative. Later X ray 8 months post., but f.b. outside of globe	2 years	O.S. L.P.	Cornea-iris perforation at "5 o'clock." Vision 20/20 for about a year, then rapid deterioration	Siderosis lentis noted at Bureau 6 months after accident. Lens track. F.b. at ora? Siderotic cataract in 1½ years
28 P.D. 45	12/12/38 Struck while hammering	Same day. F.b. extracted from lens 10 days later after daily attempts	1½ years	O.S. 20/25	Corneal perforation at "7 o'clock." Temporal iris coloboma	Capsule opacity at "7 o'clock" with implantation of iris pigment. Streaky subcapsular opacity running from it toward axis, receding in 1½ years, ⅓ corneal thickness

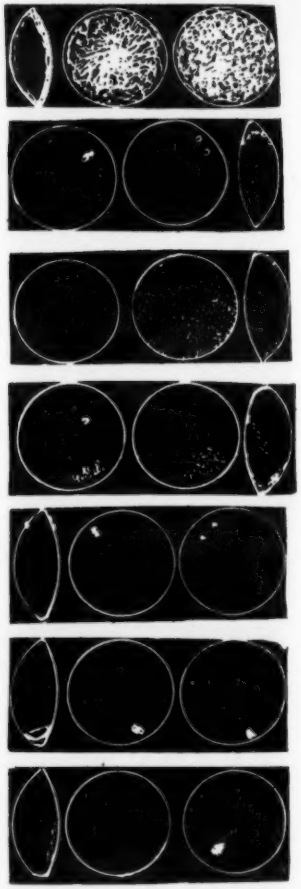
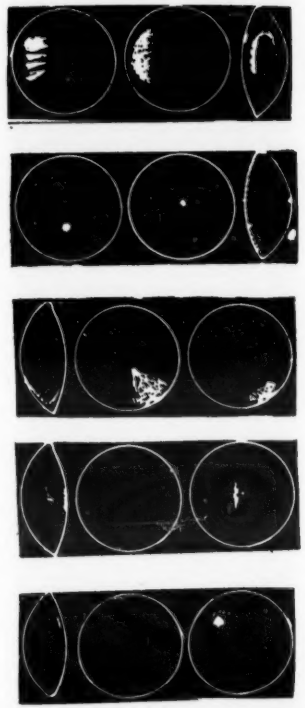


TABLE 1 (*Continued*)

Number Name Age	Date and Nature of Accident	Date of First Medical Attention. Nature of Injury	Period of Observation	End Results		
				Eye, Vision	Cornea, Sclera, Pupil, Iris, Vitreous, Fundus and Other Data	Lens Findings
29 N.S. 47	1914 In the World War	No data, except intraocular f.b. extraction—brass?	25 years	O.D. 20/20	Corneal perforation near limbus at "9 o'clock." Very small pupil as compared with fellow	Upper temporal capsule opacity, covered by iris; temporal bands of opacities with recession to level of adult nucleus and temporal posterior cortical opacity
30 R.A.H. 50	7/2/37 Electric-bulb explosion	Same day. Foreign bodies imbedded right side of face, and corneal laceration	2 years	O.D. L.P.	Corneal perforation at "6 o'clock." Gradual deterioration of vision from 20/20	Anterior axial capsular opacity, running obliquely upward to posterior capsule; f.b. lying suspended by a threadlike formation from posterior capsule. Chalcosis noted in 16 months, with greenish subcapsular dots; vitreous filled with golden dust and vivid framework. Fundus green
31 A.P. 55	6/4/38 Struck while grinding with glasses on	Same day. Subconjunctival hemorrhage and lower nasal bulbar f.b., removed	1½ years	O.S. 20/25	Cornea-iris perforation at "5 o'clock." Posterior synechia lower temporally. Vitreous opadities. Large lower temporal fundus scar	Anterior lower temporal subcapsular opacity and posterior lower temporal subcapsular with iridescent tip reaching pole
32 O.F. 55	12/6/1918 Explosion	Intralenticular f.b., extracted	21 years	O.S. 20/33	Central, irregular, deep but not demonstrably a perforation scar of the cornea	Anterior vertical capsule opacity, dense and chalky, off center nasally, a small very deep opacity lying in an annular clearing in front of anterior Y, and simulating a congenital suture opacity, except for its irregularity and faint optically more clear path leading to capsule opacity
33 H.J.A. 58	1914	No data except for intraocular f.b. extraction	25 years	O.S. 20/25–2	Cornea-iris perforation at "11 o'clock"	No capsule tear nor subcapsular cloudiness. Dense chalky mass at disjunction band

O.D.←Anterior Posterior Section
O.S.→Section Posterior Anterior



cases (nos. 7, 20, 23, 25, 27, and 30) exhibit a double lens perforation with a demonstrable track in the lens, case 23 exhibiting a capsule lesion at a distance from the end of the track as well, similar to cases reported by Meesmann. The rest either glided off the lens or may have injured the equator, perhaps on their way to an extralenticular site: in the ciliary body, vitreous, or fundus. The injury to the equator is, however, rarely demonstrable even in the cases with iris colobomata (nos. 10, 17, and 28).

Accordingly, fewer anterior-capsule opacities are observed than one would expect. In addition to the six double lens-perforation cases, there are six definite capsule opacities (nos. 1, 4, 19, 28, 29, and 32), making a total of 12 anterior-capsule perforations observed. One (no. 33) is doubtful. It is noteworthy that double lens perforations and anterior-capsule perforations are conspicuously more frequent in the older group of individuals, perhaps accounted for by capsule friability.

The majority, therefore, of lens opacities observed in this group of intraocular-foreign-body cases, except those masked by a complicating siderosis, do not differ essentially from those noted in the cases of contusion opacities. There is the same specific morphology: subcapsular beginning, segmentlike localization, the tendency to span the equator, and extend posteriorly in the direction of the posterior pole, with, however, iridescence of the tip of the posterior, more sectorlike extension. Sometimes anterior and posterior opacities, when superimposed and silhouetted, remind one of a sailboat. These features are exhibited in cases 3, 5, 8, 10, 11, 12, 13, 14, 15, 16, 17, 18, 21, 22, 24, 26, and 31; that is, in about one half of the cases, all in the adult group between the ages of 31 and 55 years. This majority of cases may be described as presenting either contusion opacities, or, because of the small size and considerable force of the object striking the lens, as perhaps concussion opacities. The senile type of contusion opacities noted in the former survey[1] do not appear among the few patients older than 50 years of age. Posterior axial and diffuse opacities are noted only in five cases (nos. 3, 11, 16, 21, and 24) and only in case 3 an anterior subcapsular axial opacity as well. The possibility that some of these contusion opacities were the result of the anterior-route extraction is to be considered. Cases 3 and 16 confirm Disler's finding of lack of continuity between axial and equatorial opacities.

The determination of the age of a lens opacity. As in the cases of contusion lens opacity, while the phenomenon of "remotio cataractae traumaticae" was noted in many cases and while a deep opacity, generally speaking, argues for age and a superficial one for recency, the rate of recession into depth was sometimes noted faster than its age alone would account for, and sometimes to have proceeded much slower than its age would lead one to expect. Such rate of recession was determined by the position of the disjunction band and the adult nucleus band and by comparison with the apparent corneal thickness of 0.4 mm. at or near the axis, rather than by the often invisible anterior Y. Thus, in case 6, complicated by siderosis and hypertension, recession as far as the disjunction band only was noted in five years, and in case 14, in which also there was hypertension, it was still at that band in nine years, in spite of the still active growth of the lens in thickness that occurs normally in these individuals, in whom generally recession is beyond the disjunction band in two years. It would seem therefore that siderosis and hypertension may retard recession. Cases 29 and 33, both seen 25 years after injury,

are particularly instructive. While in the first case, in which the injury occurred when the patient was 22 years old, there was the expected recession to a deep level of the adult nucleus, in the second case, the injury occurring at the age of 33 years, there was recession only as far as the disjunction band. Capsule rupture, which means penetration of lens to a varying depth, would seem to make particularly for a varying rate of recession. Thus while in cases 7 and 19 recession to the disjunction band was noted in 1 year and 6 months, respectively, in case 28 it had progressed in 1¼ years to one corneal thickness, or quite beyond the disjunction band. In case 25 a recession-of-capsule opacity was noted as far as the disjunction band only in 4 years. In case 32, with corneal perforation no more demonstrable after 21 years, the extremely deep recession simulated a congenital suture opacity.

The Prognosis. The end results may be considered good in about two thirds of the cases, with vision better than 20/40 and not perceptibly affected by the age of the individual. The lens opacities in the main are small and stationary in this group that has a favorable outcome. Deterioration after a stationary period of about nine years occurred once, in case 14.

The causes of poor results leading to industrial blindness in 13 of the cases may be summarized as follows:

6—overlooked, with siderosis
2—overlooked, with chalcosis
1—overlooked, because of poor X-ray examination, with siderosis
1—extraction not successful
3—extraction with later complications (detachments, hypertension, and cataract)

It would appear, therefore, that at least 50 percent of the poor results could also have been prevented. The prognosis may thus be said to be potentially good in 75 to 80 percent of the type of intraocular-foreign-body cases here considered; that is, in those not immediately bad. The causes of their being overlooked, aside from the cases not handled by an ophthalmologist, in the first place, may be seen to lie in scleral, poorly visible and identifiable perforations; reliance on poor X-ray studies; lack of the use of the slit-lamp; and incomplete exploration of the fundus periphery.

The first records of the observation of siderosis were: in case 2 on the eighteenth day, in the others after an interval varying from 6 months to 2 years. It should be noted, however, that the first recorded observation of siderosis is not at all necessarily its first appearance, nor the first possibility of its being diagnosed as siderosis lentis. Attention is called to the condition only by the slow deterioration of vision which brings back a claimant to the ophthalmologist. This may not be appreciable until several months after he had been discharged from observation.

The cases of chalcosis have been observed from the beginning by the writer and in one case was first noted 16 months and in the other 17 months after entry. It would appear that chalcosis is a slower process than is siderosis. In neither case was there a sunflower appearance.

Lens lesions in ocular ruptures

In this group the responsible agent is larger and the force more considerable than in the intraocular-foreign-body group. In addition to the rupture we encounter phenomena of laceration and contusion, particularly in cases of partial scleral rupture, often regarded merely as contusions. It was considered appropriate to include such cases of partial scleral ruptures and of the small limbic ruptures of Fuchs. The special features with bearing on the pathogenesis of the lens lesions

TABLE 2

LENS LESIONS IN OCULAR RUPTURES

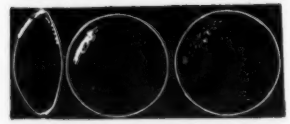
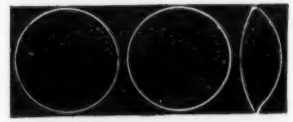
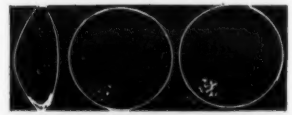
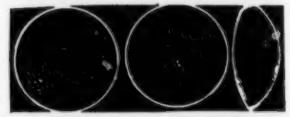
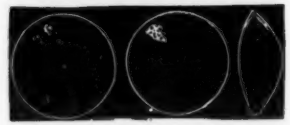
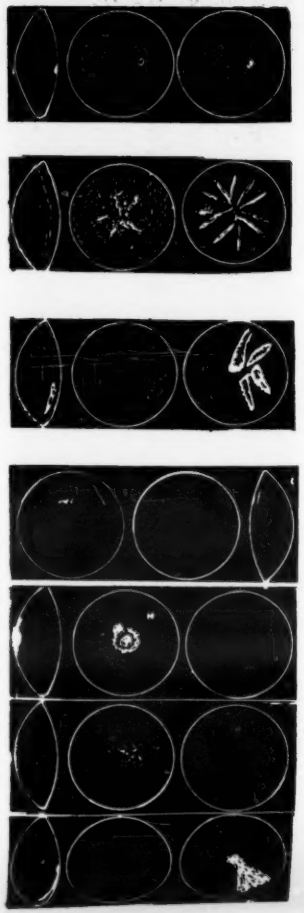
Number Name Age	Date and Nature of Accident	Date of First Medical Attention. Nature of Injury	Period of Observation	End Results			O.D.←Anterior Posterior Section O.S.→Section Posterior Anterior
				Eye, Vision	Cornea, Sclera, Pupil, Iris, Vitreous, Fundus and Other Data	Lens Findings	
1 M.D. 22	2/27/39 Glasses broken by vise handle	Same day. Laceration upper lid and cornea with iris prolapse. Glass in anterior chamber removed by peripheral iridectomy. Lens opacity noted in 3 weeks	1 year	O.D. 20/33 +	Upper nasal-perforation scar of cornea; coloboma with anterior synechiae	Upper temporal epicapsular congenital pigment. Upper nasal subcapsular opacities with recession to disjunction band in 10 months	
2 M.M. 24	12/20/38 Cable snapped and struck lid	Same day. Nasal upper lid and lower lid laceration and ruptured globe. 4 mos. later hypertension. 8 mos. later iridectomy	1 year	O.S. 20/33 to 20/40 with mixed 1.50 D. astig.	Upper lid-border scar. Upper nasal keratoplasty. Upper nasal iridodialysis. Vitreous pigment. Retinitis proliferans below. Glaucomatous cupping	Upper nasal anterior punctate subcapsular opacities. Upper nasal posterior epicapsular pigment	
3 W.H. 25	4/17/39 Struck while driving nail	Same day. Iris prolapse	½ year	O.D. 20/66	Upper nasal-perforation scar of cornea and iris atrophy with anterior synechiae	Sectorlike anteroposterior subcapsular opacities, posterior one reaching to pole	
4 G.G. 29	7/13/37 Struck by nail	Same day. Perforation of cornea, iris, and lens	2½	O.S.	Perforation scar of cornea and anterior synechiae lower nasally	Lower nasal anteroposterior subcapsular opacities	
5 McN. M. 29	12/13/37 Struck by wire	Same day. Temporal conjunctival perforation; iritis and vitreous opacities	2 years	O.D. 20/50	Pigmented scleral scar over ciliary body at "8 o'clock." Lower temporal posterior synechia. Vitreous opacities. Temporal fundus scarring	Anterior lower temporal subcapsular opacity. Posterior epicapsular lower temporal pigment. Subcapsular posterior iridescence below pole	
6 M.G. 30	2/17/39 Struck by something from a passing truck	Same day. Conjunctival hemorrhage. Corneal laceration. X ray negative	1 year	O.D. 20/20	Stellate perforation scar of cornea at "10 o'clock" and posterior synechiae, radial iris transillumination at "11 o'clock," upper temporal heavy pigment masses in fundus	Upper temporal anterposterior subcapsular opacities	

TABLE 2 (*Continued*)

Number Name Age	Date and Nature of Accident	Date of First Medical Attention. Nature of Injury	Period of Observation	Eye, Vision	End Results: Cornea, Sclera, Pupil, Iris, Vitreous, Fundus and Other Data	End Results: Lens Findings
7 S.M. 33	12/10/38 Struck by nail	Same day. Central corneal perforation	1 year	O.S. 20/25	Stellate corneal perforation scar, at "3 o'clock"	Capsular opacity at "3 o'clock" on border of pupillary zone. Posterior large subcapsular vacuole in direct line with corneal and anterior capsular scar and strikingly like latter in form. No anteroposterior track discernible
8 A.Ch. 35	10/2/38 Struck by customer	Same day, by gen. pract., 2 weeks later ophth. noted evidence of hypotension and retinal and choroidal ruptures	1 year	O.S. 20/50	Small partial upper equatorial scleral rupture. Upper choroidal ruptures. Pigmented macula. Upper extreme fundal periphery suggestion of retinal detachment, or perhaps choroidal	Anterior subcapsular opacity at "9 o'clock." General widening of all cortical sutures so that stellate lens opacity is simulated. Marked widening of anterior disjunction zones suggestive of intumescence. Posterior polar ground-glass appearance and iridescence
9 P.S. 35	3/5/38 Struck by piece off chisel	Same day. Incised temporal ciliary-body wound. Hematoma	2 years	O.S. 20/20	Temporal ciliary-body scar. Iris perforation at "3 o'clock," deformed pupil	Temporal subcapsular anterior opacity receding to disjunction band in 1 yr. overlying wide radial striae thicker axially. Epicapsular post. pigment; 1 yr. later recession to slightly beyond disj. band, perhaps to ¼ corneal thickness and disappearance of thick striae
10 F.J. 40	5/20/39 Struck by nail	Next day. Laceration of cornea. Traumatic cataract	1 year	O.D. 20/33	Upper temporal corneal perforation	Hour-glass formation of anterior epicapsular congenital brownish dots, also present in O.S. Upper horizontal capsule opacity with recession into cortex in 1 year
11 F.A. 40	1/18/39 Struck by stone	Same day. Iris prolapse. Traumatic cataract	1 year	O.S. 20/60	Lower nasal cystoid limbus scar and coloboma of iris. Vitreous pigment	Upper temporal posterior equatorial subcapsular opacity. Posterior polar large cystlike opacity, suggestive of the "oil drop with saturn ring" appearance of a lenticonus posterior when first seen. Its true nature indicated 6 months later when the apparent cyst had collapsed into merely a large irregular axial subcapsular opacity, as shown in 2d illustration
12 C.P. 42	3/23/39 Struck by porcelain off cable	Same day. Corneal laceration. Prolapsed iris, excised	1 year	O.S. 20/25	Meridional corneal laceration at "4 o'clock," from center to limbus. Lower temporal operative coloboma	Anterior axial capsule perforation and sectorlike subcapsular opacity lower temporally

O.D.←Anterior Posterior Section
O.S.→Section Posterior Anterior



13 R.A. 41	6/13/38 Struck by needle	Same day. Corneal perforation	1½ years	O.D. 20/25	Stellate corneal perforation and anterior synechiae at "6 o'clock"	Hook-shaped anteroposterior subcapsular opacity with recession in 1½ years to disjunction band. No track, but post. tip of opacity strikingly similar in form and in line with anterior opacity
14 B.C. 41	10/14/37 Struck by wire	Same day. Deep corneal abrasion	2 years	O.S. 20/20	Corneal perforation scar at "6 o'clock" within pupillary zone	Anterior subcapsular opacity at "2 o'clock" under iris
15 B.Ph. 41	12/4/36 Struck by harness buckle	Next day. No data	3 years	O.S. 20/20	Limbus perforation at "3 o'clock." Larger round pupil. Meridional choroidal atrophic patch at "3 o'clock" in periphery	Posterior polar subcapsular opacity with meridional opacities posteriorly
16 D.J. 44	12/8/38 Struck by wire	Same day. Corneal perforation. Iris prolapse, excised	1 year	O.S. 20/20	Corneal perforation scar and operative coloboma temporally	Anterior axial subcapsular punctate opacities
17 LoP.? 45	1/9/38 Struck by nail	Same day. Upper temporal corneal and iris perforation. Anterior synechiae	2 years	O.D. 20/20–2	Upper temporal cornea and iris perforation	Upper temporal subcapsular anteroposterior meridional opacities.
18 L.G. 45	9/24/37 Struck while cleaning boiler	Next day. Corneal perforation. Striped keratitis and cyclitis	2 years	O.S. 20/25	Central corneal perforation	Anterior axial subcapsular rosette-shaped opacity with recession in 2 years to disjunction band only
19 M.? 45	8/2/37 Spring broke glasses	Same day. Corneal laceration. Lens opacity noted 10 weeks later	2½ years	O.D. 20/66	Corneal perforation at "6 o'clock"	Anterior axial subcapsular lens opacity

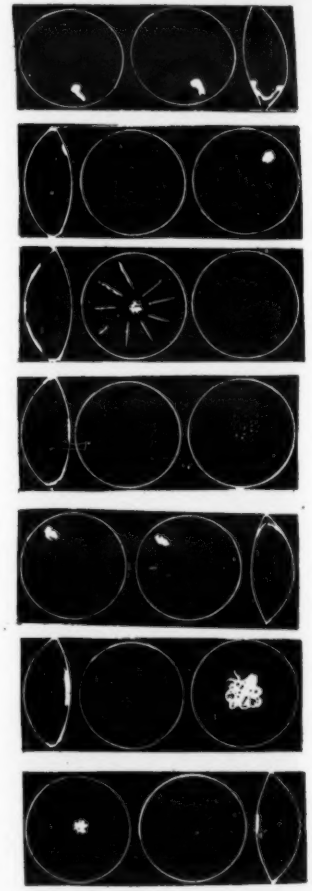
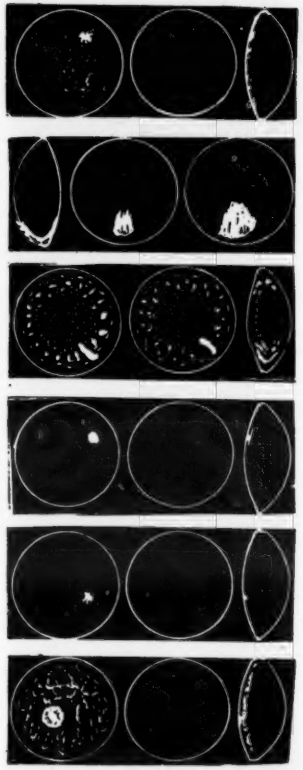


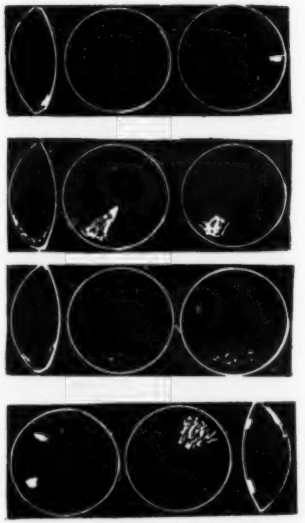
TABLE 2 (*Continued*)

Number Name Age	Date and Nature of Accident	Date of First Medical Attention. Nature of Injury	Period of Observation	End Results		
				Eye, Vision	Cornea, Sclera, Pupil, Iris, Vitreous, Fundus and Other Data	Lens Findings
20 Y.R. 45	8/15/27 Struck by nail	Same day. Irregular pupil. Lens opacity	12 years	O.D. L.P.	Upper nasal deep corneal scarring, difficult to demonstrate as perforation. Case closed in 1928 with a vision of 20/50. Sudden deterioration in 1939	No original data on lens available. Now complete cataract. Note upper nasal-capsule opacity
21 S.C. 46	12/7/31 Struck by nail	Same day. No other data	8 years	O.S. L.P.	Lower temporal corneal and iris perforation. Case closed in 1932 with a vision of 20/25. Sudden deterioration recorded as in the 1st few months of 1939	Original lens findings were anteroposterior subcapsular opacities and posterior epicapsular pigment. Now complete cataract
22 R.G. 45	11/3/19 Struck by wire	No data	20 years	O.D. 20/20–3	Corneal and iris perforation at "5 o'clock"	Hook-shaped lower nasal cortical anteroposterior opacity combined with typical zonular and cerulean and coronary lens opacities and dilacerated anteroposterior opacities in front of fetal sutures. O.S. lens clear
23 O.S. 49	10/13/38 Struck by corner of level	Contusion. Subconjunctival scleral rupture. Hemorrhage into anterior chamber. Prolapsed iris and ciliary body	2 years	O.D. L.P.	Corneal scars O.U. not related to present accident. Upper nasal scleral rupture. Hypotony. Subluxated lens. Coloboma of iris. Fundus normal at first, 10 months later detachment	Upper nasal anterior subcapsular opacity with recession to disjunction band in eight months, and anterior subcapsular vacuolization following detachment
24 H.A.A. 50	5/15/39 Struck by nail	Same day. Corneal perforation	½ year	O.D. 20/50	Horizontal corneal perforation	Stellate capsular opacity at "4 o'clock." Subcapsular opacity recessed to disjunction band in six months
25 T.D. 52	11/15/38 Glasses broken by piece of brass	Same day. Corneal and lens laceration and glass in anterior	1 year	O.D. L.P.	Temporal corneal perforation and coloboma	Anterior zonule fibers broken. Capsular perforation with iris inclusion at "8 o'clock"

O.D.←Anterior Posterior Section
O.S.→Section Posterior Anterior



26 H.J. 52	6/17/37 Struck by wire	3 days later. Corneal and lens perforation	2½ years	O.S. 20/33	Limbus perforation at "3 o'clock"	Temporal anterior capsular opacity
27 M.H. 53	3/8/39 Struck by wire	Same day. Hyphemia. Feathery lens opacity noted two weeks later	1 year	O.S. 20/66	Perforation of cornea and iris at "5 o'clock." Posterior synechiae at "6 o'clock." Pigment in vitreous	Posterior feathery axial opacity reported observed 2 weeks after injury to disappear later. Anteroposterior subcapsular opacity at "7 o'clock" with posterior tip iridescent
28 H.J. 57	10/11/37 While hammering struck by hard piece of paint	Next day. Corneal foreign body extracted. A few days later, corneal perforation and lens opacity noted	2 years	O.D. 20/25	Corneal perforation at "7 o'clock"	Anteroposterior subcapsular opacities below
29 G.G. 60	9/7/38 Struck by broken handle	Same day. Lid laceration. Subconjunctival hemorrhage, vitreous hemorrhage, lens subluxation	2 years	O.D. 20/30	Upper nasal concentric scleral rupture, deformed pupil, pupillary border notchings at "6, 8 and 11 o'clock." Upper temporal extensive pigmented chorioretinal scar, upper nasal large retinal cyst, massive vit. pig., subchoroidal hemorrhage, hypotension O.D. 17 mm.	Epicapsular pigment anteriorly at "10 and 8 o'clock," and small subcapsular opacities at disjunction band; posterior streaky opacity upper nasally at disjunction band, first seen as a hemorrhagic deposit



characterizing them are the brief but considerable hypertension which must accompany them before the globe is opened and perhaps for some time afterwards, because of hemorrhage, and the subsequent either transient or persistent hypotony following the opening of the globe which may supervene.

This group (data regarding which are condensed in table 2) includes 15 right eyes and 14 left eyes. The age distribution, however, is quite different from that found in the preceding group, possibly due to special occupational age-selection factors.

The nature of the accident was mainly the being struck by the end of a wire or by the recoil of a nail.

In 22 cases (80 percent) the ruptures were corneal, 16 cases among them including iris involvements, synechiae, and operative colobomata. In six cases the ruptures were either at the limbus or in the sclera. The corneal scars were characteristically stellate, irregular, and splintered, and readily distinguished from the clear-cut perforations with retention of the intraocular-foreign-body group when recent. Case 20, however, shows the difficulty of identifying them when old, in this case 12 years. The limbic and scleral group are either direct or indirect or only partial and incomplete ruptures, with one case of hypertension (case 2) and three cases of hypotension among them (cases 8, 23, and 29), and one (case 23) with detachment—all evidently related to subchoroidal and subretinal hemorrhages.

Among the lens lesions there are only 7 capsule perforations (cases 7, 10, 12, 20, 24, 25, and 26). Their preponderance among the more aged individuals is, however, of less significance than it is in the intraocular-foreign-body group, given the anomalous age distribution in the ocular-rupture group.

The rest of the lens lesions are morphologically essentially contusion-lens opacities, as has also been noted in the majority of the foreign-body group. Attention is called to cases 8, 9, and 15 and their similarity to case 38 in the contusion study, all scleral or limbus perforations. The appearance and disappearance of the radial striations suggests a reversible aqueous-imbibition process in case 9, and case 38 of the contusion study. Case 11 is instructive in that a formation strikingly similar to a lenticonus posterior was observed to have evolved into a flat subcapsular opacity. Duverger and Velter[15] have recently pointed out that lenticonus posterior may mean capsule rupture. In case 18 the characteristic juvenile rosette formation was observed in a person of 45 years. Case 22 is also worth noting in that uniocular zonular - coronary - cerulean opacities, heretofore only associated with contusions, were observed in a person of 45 years, the result of an ocular rupture at the age of 25. Posterior axial involvement was noted in cases 5, 8, 11, and 15—all scleral-rupture cases. A transient feathery star-shaped posterior opacity was recorded in case 27.

In regard to the recession rate of subcapsular opacities, more regularity was observed, and where noted recession within two years did not pass the disjunction band, regardless of the age of the individual. Only in case 10 was recession more rapid, and in case 22 evidently retarded. Acceleration of recession in case 8 was noted, probably related to the hypotension.

The outcome was quite favorable in about two-thirds of the cases. The four cases of industrial blindness were all in persons over 40 years of age. Two deteriorations after a stationary period of 12 years (case 20) and 8 years (case 21) took place at the age of 45 years, the critical period apparently for such deteriorations.

Conclusions

1. A survey of 62 lens lesions, primarily opacities, observed in cases of eye perforations by intraocular foreign bodies and in eye ruptures without retention of foreign body, indicates that the majority are the result of lens contusion and morphologically belong to the type of contusion lens opacities previously studied. Posterior feathery star-shaped opacities are evidently rare.

2. Capsule perforation, lens penetration, or its double perforation occur in less than a third of the cases that do not lead to immediate cataract.

3. The retrospective diagnosis of the eye perforation or rupture origin of a lens opacity is sometimes made difficult because of the eventual blurring of the perforation or rupture character of a corneal scar after many years and particularly because of the difficulty in diagnosing an older partial limbus and scleral perforation or rupture.

4. The rate of recession into the depth of the lens of originally subcapsular opacities is found to vary in this study just as in the study of pure contusion lens opacities. The factors affecting the rate seem to be: capsule lesions, which tend to retard it; varying depth of lens penetration, which would tend to accelerate it; hypertension and siderosis, which tend to retard it; and hypotension, which favors it.

5. As to the evolution of the lens lesions in this mild variety of cases, the end results are satisfactory in the majority of cases, but prognosis should be more guarded in the individual after he is 30 years old. Deterioration should be watched for in the fifth decade, when apparently most deteriorations occur.

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THE PHARMACOLOGICAL BEHAVIOR OF THE INTRAOCULAR MUSCLES*

II. Sensitization phenomena in the dilator and sphincter iridis

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In the first paper of this series (Sachs and Heath, 1940), we set forth certain concepts and procedures which we consider essential for an attack on the problem of the nature and efficacy of drug sensitization in smooth muscles, with particular reference to those of the eye; namely, (1) Determine the maximally effective concentration (M.E.C.) of each drug, and with such concentrations as stimuli: (2) Determine work outputs at definite loads. One is then able to: (3) Discriminate sensitization from the summation of drug effects and can: (4) Determine whether the sensitization is of the "threshold" type, in which the presence of one drug makes possible a degree of response to a given concentration of a second drug which would otherwise be given only to a higher concentration, and can: (5) Determine whether the sensitization is of the "augmentative" type, wherein the response to the combination of synergistic drugs in M.E.C. concentrations is greater than that to either drug alone in any concentration. With this information, one can: (6) Take the quotient of high-load amplitude over low-load amplitude as a criterion of stimulus-strength, and by comparing the quotients obtained with M.E.C. dosages, with and without sensitization: (7) Express the strength of one drug or combination relative to that of another drug or combination.

In comparisons of the responses to two or more stimulus-situations we have, wherever possible, made the comparison on a single strip of tissue which was washed between tests. This minimizes the necessity for ever comparing the performance of one strip under one set of conditions with that of another strip under other conditions, effecting a great economy of effort since any statistical treatment of large numbers of these highly individualistic preparations is obviated.

With the above considerations in mind, we have studied the action of various drugs on strips of albino rabbit iris, with apparatus and technique already described (Sachs and Heath, 1940). The present contribution reports experiments with cocaine and adrenaline on the dilator, and acetylcholine and eserine on the sphincter.

The adrenaline-cocaine-dilator system

Determination of M.E.C. of adrenaline. Twenty-four experiments were made with 20-mg. and 140-mg. loads. Graph *A* in figure 1 shows a sample experiment, made with a 20-mg. load. The first test of the strip (solid tracing, as in all the graphs in figure 1) shows the result when adrenaline in 1:1,000,000 concentration was supplied, followed later by an additional dose containing the same absolute amount of drug. The second dose, it will be noted, elicited a further contraction, the total amplitude due to the two applications being 1.45 scale units.

After washing, the preparation returned to its previous starting level in a few minutes, and then yielded a second tracing (dotted line) in which a full con-

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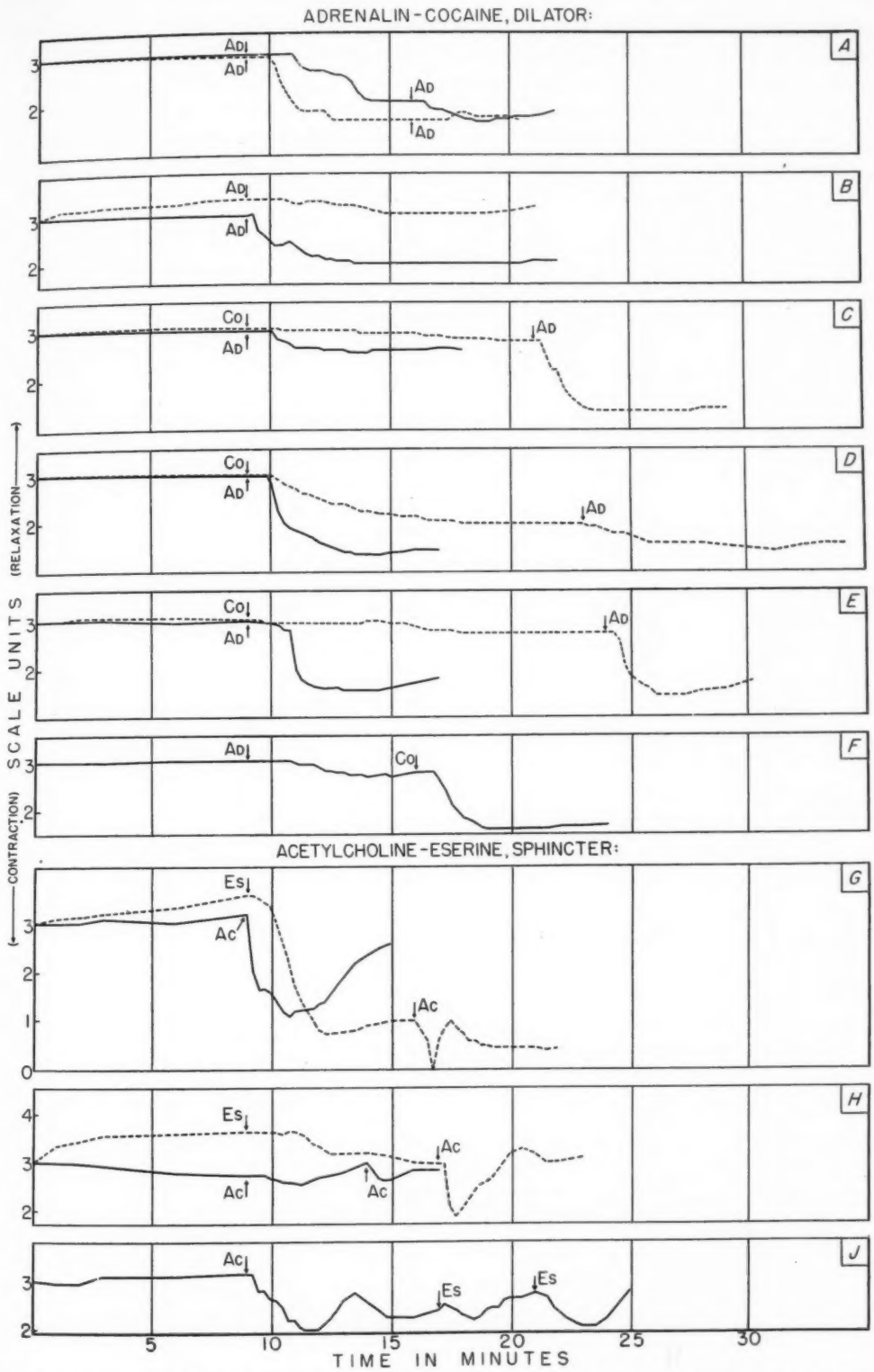

Fig. 1 (Sachs and Heath). Sample tracings obtained from albino-rabbit iris-muscle strips under drug stimulation. Explanation in text.

traction was given to an initial dosage equalling the two dosages of the first test. The second dosage supplied was equal to the initial one, but called forth no further contraction. This initial dosage of the second test (1:500,000) is, by itself, making it necessary to exclude summative effects. Its action was peculiar, in that it caused no contractions in low concentrations (or, as a rule, in high ones). We adopted a concentration of 1:500,000 as being reliable for producing

TABLE 1

BEHAVIOR OF 11 DILATOR STRIPS TOWARD COCAINE AND ADRENALINE

Strip		Amplitude of contraction, scale units, to:				Shown in Fig. 1, in
		(Before washing)	(After washing)		Both drugs, total	
		Adrenaline, alone	Cocaine, 1:500,000	Adrenaline, additional		
	1	(1:50,000,000) 0.35	0.50	(1:50,000,000) 1.35	1.85	
	2	(1:50,000,000) 0.45	0.25	(1:50,000,000) 1.45	1.70	Graph *C*
	3	(1:500,000 = MEC) 1.60	0.80	(1:50,000,000) 0.55	1.35	
	4	(1:500,000 = MEC) 1.65	1.00	(1:50,000,000) 0.55	1.55	Graph *D*
	5	(1:500,000 = MEC) 0.85	0.45	(1:50,000,000) 0.35	0.80	
	6	(1:500,000 = MEC) 1.70	0.65	(1:500,000 = MEC) 1.20	1.85	
	7	(1:500,000 = MEC) 1.40	0.25	(1:500,000 = MEC) 1.30	1.55	Graph *E*
	8		0.05	(1:100,000,000) 0.30	0.35*	
	9		0.20	(1:100,000,000) 0.40	0.60†	
Reversed order of application	10	(1:500,000 = MEC) 1.70	0.80 ←	(1:5,000,000) — 1.05	1.85	
Reversed order of application	11		1.10 ←	(1:50,000,000) — 0.35	1.45	Graph *F*

* Increased to 1.00 unit by subsequent treatment with M.E.C. adrenaline.
† Increased to 1.60 units by subsequent treatment with M.E.C. adrenaline.

then, the M.E.C. for this load. It was found that this dosage was also M.E.C. for 140 mg., though to be on the safe side we used 1:333,333 in a few experiments, 1:500,000 in most, without finding significant differences.

The character of cocaine-adrenaline sensitization. Cocaine elicits contractions contractions, which were of a slow type. A slow contraction is not specifically characteristic of any one drug. In the experiment illustrated in graph *B*, figure 1, the first test was made with M.E.C. adrenaline and a 20-mg. load, producing a characteristic, fairly rapid shortening. In the second test the load was 140 mg.,

and it will be noted that the contraction was slower as well as of much less amplitude.

The synergic action of cocaine and adrenaline was studied in 10 experiments which are tabulated in table 1, samples being illustrated in graphs *C-F* in figure 1. On strips 1 and 2, adrenaline in sub-M.E.C. dosage (1:50,000,000) was used first, producing contractions of 0.35 and 0.45 scale units, respectively. After washing, each strip was supplied with 1:500,000 cocaine, the single effect of which was to evoke contractions of 0.50 and 0.25 scale units, respectively. Following the stabilization of the cocaine contractions, the same weak (1:50,000,000) adrenaline was given, yielding additional contractions of 1.35 and 1.45 scale units, giving total contractions of 1.85 and 1.70 scale units in the respective strips. One of these experiments is shown in graph *C*. It clearly demonstrates that the combined effect of the two drugs (1.70 units of amplitude) is greater than the sum of their single effects (0.25 + 0.45 = 0.70 units). Summation is thus ruled out, and the occurrence of true sensitization confirmed.

In three experiments (on strips nos. 3, 4, and 5, exemplified in graph *D*) the effect of cocaine combined with sub-M.E.C. adrenaline was compared with that of M.E.C. adrenaline alone. The strong adrenaline used first, produced contractions of 1.60, 1.65, and 0.85 scale-units amplitude, respectively. Total contractions to an initial dose of cocaine, followed later with 1:50,000,000 adrenaline, were not greater—1.35, 1.55, and 0.80 units, respectively (see table 1). The suggestion here is that the sensitization is of the threshold type.

This was confirmed by two experiments (strips 6 and 7, one of them shown in graph *E*) in which the effect of M.E.C. adrenaline was compared with that of cocaine plus M.E.C. adrenaline. The amplitudes to adrenaline acting singly were 1.70 and 1.40 units, those to the combined drugs not significantly higher (1.85 and 1.55 units). The dotted tracing of graph *E* brings out the relay-race effect in the combined action. Cocaine, then, cannot increase the effect of M.E.C. adrenaline, and the sensitization is consequently of the threshold type, not the augmentative.

The threshold concentration of adrenaline having been found, in several experiments, to be about 1:100,000,000, the ability of cocaine to sensitize to this weak dosage was tried out on two strips (nos. 8 and 9 in table 1). On the first of these, cocaine produced a 0.05-unit contraction, liminal adrenaline increasing this only to 0.35 units. The corresponding amplitudes in the second strip were 0.20 and 0.60 units. These "sensitized" values are so far short of those yielded by M.E.C. adrenaline or by cocaine plus 1:50,000,000 adrenaline (see graph *C*) that it is obvious that the capacity of cocaine to sensitize to liminal adrenaline dosages is slight. Both of these strips were tested for normality with M.E.C. adrenaline, which raised the "sensitized" contraction of 0.35 units to 1.00 unit, and in the other strip increased the amplitude from 0.60 units to 1.60.

In two more strips (nos. 10 and 11 in table 1) the effect of reversing the order of application of the two drugs was tested. One of these experiments (strip no. 11) is illustrated in graph *E*. Adrenaline in sub-M.E.C. concentration (1:50,000,000) was applied first and produced the expected small contraction (compare the solid tracing in graph *C*). When cocaine was now added, a considerable contraction ensued, to an amplitude comparable with that produced when, as

in the experiment shown by the dotted tracing of graph *C*, the cocaine is given first and the adrenaline subsequently. The order of application thus makes no difference with this particular pair of synergistic drugs.

Preliminary experiments with the synergic combination of cocaine and adrenaline, not described here in detail, showed that amplitude is again a linear function of the load as with adrenaline acting alone. The behavior of 10 strips toward 20-mg. and 140-mg. loads, under the sensitization stimulation, was then studied. The results are tabulated in table 2 and are depicted graphically in figure 2.

TABLE 2

SENSITIZED RESPONSES OF 10 DILATOR STRIPS TOWARD LOW AND HIGH LOADS

Strip	Concentration		Load, mg.	Amplitude of contraction, scale units, to			High-load ampl. / Low-load ampl.
	Cocaine	Adrenaline		Cocaine	Adrenaline, additional	Both drugs, total	
1	1:100,000 1:100,000	1:500,000 1:500,000	20 140	0.20 0.00	0.80 0.15	1.00 0.15	.150
2	1:500,000 1:500,000	1:500,000 1:500,000	20 140	0.75 0.00	1.00 0.25	1.75 0.25	.143
3	1:500,000 1:500,000	1:500,000 1:500,000	20 140	0.65 0.00	1.35 0.75	2.00 0.75	.374
4	1:500,000 1:500,000	1:50,000,000 1:50,000,000	20 140	0.25 0.00	1.45 0.15	1.70 0.15	.089
5	1:500,000 1:500,000	1:50,000,000 1:50,000,000	20 140	0.80 0.00	0.55 0.25	1.35 0.25	.185
6	1:500,000 1:500,000	1:50,000,000 1:50,000,000	20 140	1.00 0.00	0.55 0.20	1.55 0.20	.129
7	1:500,000 1:500,000	1:333,333 1:333,333	20 140	0.60 0.00	0.15 0.25	0.75 0.25	.333
8	1:500,000 1:500,000	1:500,000 1:333,333	20 140	0.90 0.00	0.25 0.15	1.15 0.15	.130
9	1:500,000 1:500,000	1:500,000 1:500,000	20 140	0.00 0.00	0.70 0.02*	0.70 0.02	.028
10	1:500,000 1:500,000	1:5,000,000 1:5,000,000	20 140	0.20 0.00	1.45 0.25	1.65 0.25	.151

* Extrapolated value—actual load was 125 mg.

Relative strength of adrenaline and cocaine plus adrenaline. In the preceding paper (Sachs and Heath, 1940) it was shown that for a range of loads from 20 mg. to 140 mg., the amplitude of contraction of dilator strips is a linear function of the load under adrenaline in M.E.C., and that for this drug the strength index (high load amplitude divided by low load amplitude) is about 0.245.*

A majority (6) of the 10 strips gave high-low amplitude quotients between 0.110 and 0.200, two strips falling below this modal group (0.00 to 0.100), and two above it (0.310 to 0.400). These six strips yielded graphs converging upon an extrapolated maximal elevable load of about 160 mg., as seen from figure 2. Their

* With our particular standard width of strip, as regulated by the width of our clamps.

quotients average 0.148.

The relative strengths of adrenaline singly, and adrenaline plus cocaine, as stimuli, are compared graphically in figure 3, in which the contractions under low (20-mg.) loads have both been set equal to 100 percent, the better to point the contrast between the two stimuli. From the data given in our earlier paper (Sachs and Heath, 1940—see especially figure 5) adrenaline is shown as yielding a "strength criterion" of 24.5 percent, predicting (with the width of strip used) a maximal elevable load of 180 mg. Although cocaine plus adrenaline is, as we have shown above, a sensitization-com-

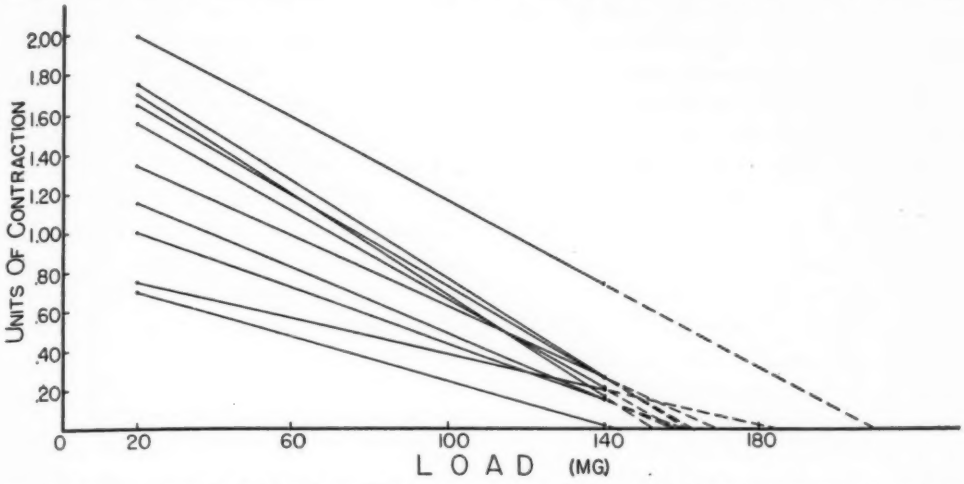

Fig. 2 (Sachs and Heath). Load-amplitude graphs of 10 albino-rabbit dilator strips under cocaine-adrenaline stimulation, with low and high loads. Explanation in text.

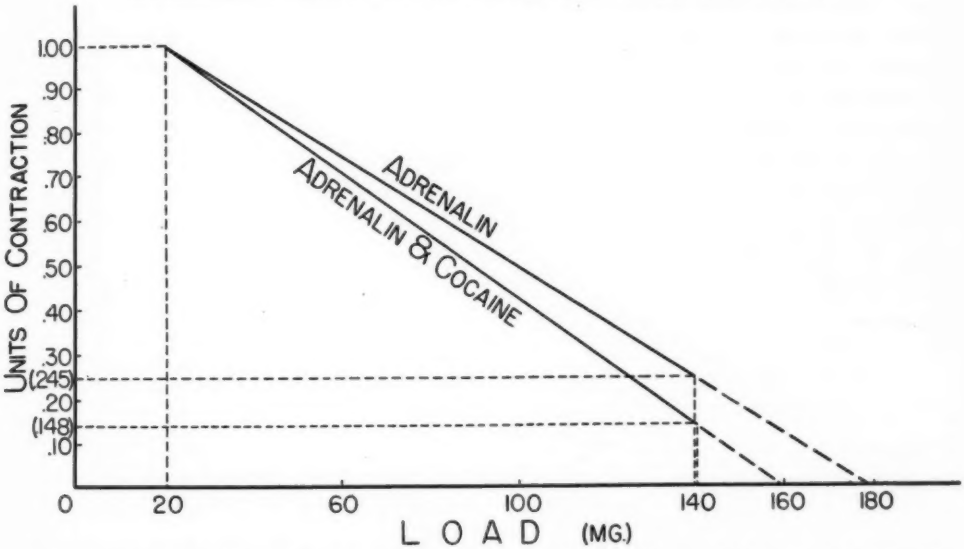

Fig. 3 (Sachs and Heath). Comparison of strengths of adrenaline, and adrenaline plus cocaine, as stimuli for the albino-rabbit dilator. The low-load amplitudes have been set equal to 100 percent, so that the high-load amplitudes directly reveal the high-low amplitude quotients and the slopes of the graphs bring out the disparity in maximal elevable load. Further explanation in text.

bination of the threshold type, the muscle under the drive of this combination does not do quite so well. The strength of the paired drugs as a stimulus is expressed by the quotient 14.8 percent, and the indicated maximal elevable load is significantly lowered (to about 160 mg.).

Thus, although cocaine increases the effect of sub-M.E.C. concentrations of adrenaline under small loads, and the amplitude of contraction under the combined drugs equals that under adrenaline alone, the combination is not so effective when the muscle is asked to overcome a high resistance. There is clear evidence here that cocaine decreases the working capacity of the adrenaline-dilator system. Considering the properties of cocaine, it is reasonable to suppose that this reduction is an expression of toxicity.

Though "sensitization" and "increased effect" are commonly regarded as practically synonymous, our results in the case of cocaine-adrenaline show the need of carefully examining the extent and limitations of the "increased effect" in any given instance of pharmacological sensitization. We feel that an absolute essential to such careful examination is the study of response to high loads and the computation of comparative high-low amplitude quotients.

The acetylcholine-eserine-sphincter system

Determination of the M.E.C.'s of the two drugs. The maximally effective concentration of acetylcholine was determined on 18 sphincter strips by the general method outlined above for adrenaline in its action on the dilator. With a load of 140 mg., maximal responses were found to be given to concentrations of 1:50,000 to 1:40,000, which were also regarded as M.E.C. in experiments with 20-mg. loads. During this work with split dosages, it was found that the second dosage could be given either during contraction to the first, or during the subsequent relaxation, with the same end result as to the maximal amplitude attained.

On 13 strips, similar determinations were made of the M.E.C. of eserine, which was also found to range from 1:50,000 to 1:40,000.

Load-amplitude relationships. To neither of these drugs—and particularly eserine—is the sphincter by any means as regular in its response as is the dilator under adrenaline or even under cocaine. Certain items of the ideal procedure outlined at the commencement of this paper had consequently to be modified or even omitted. Each drug was studied with the preparation under various loads from 20 mg. to 140 mg., but it sometimes happened that the amplitude of contraction under eserine was higher under a high load than under the lowest one. This variability made it impossible to plot a meaningful load-amplitude curve for even a single strip—let alone by averaging strips, which procedure we have striven to avoid. And, of course, no "maximal elevable load" could be suggested by extrapolation.

Even under acetylcholine, the action of which is far more predictable than that of eserine, we could obtain no clear evidence that the amplitude and load were related in a linear fashion over the 20-mg. to 140-mg. range convenient for experimentation with our particular muscle-clamps and recording apparatus. In great contrast to the steady behavior of the dilator toward adrenaline dosages, sphincter preparations sometimes failed to contract at all under high drug concentrations, while at other times they responded to weak dosages as if the latter were of M.E.C. strength.

However, in order to be able to express in a rough way the relative effectiveness

of the "physiological" stimuli, adrenaline and acetylcholine, upon their respective appropriate effector organs, the dilator and sphincter, we did test nine favorable sphincter strips under 20-mg. and 140-mg. loads. Six of these yielded work-output quotients (as given by the ratio of high- to low-load amplitudes) ranging from 0.100 to 0.200 with an average of 0.159. One strip gave a value below this range, the other two being above. This rough value of 0.159 is to be aligned with the comparable, higher, and more accurately determined quotient of 0.245 for the effectiveness of adrenaline upon the dilator.

Considering the circumstances, it was naturally impossible to apply the method of maximal load and high-low amplitude quotient for any close determination of the relative effectiveness of the acetylcholine-eserine combination. Further study of this synergism consequently extended only to an assignment of the sensitization involved to its proper category in our classification.

The character of acetylcholine-eserine sensitization. Inasmuch as each of these drugs singly is a powerful stimulant of the sphincter, neither can well be designated as the "primary" drug and the other as the "sensitizer," except, perhaps arbitrarily, in a particular experiment in which one drug is used in low concentration.

Preliminary experiments on seven sphincter strips had revealed a peculiar, extensive, and twitchlike contraction to acetylcholine following pretreatment with eserine. The extent of this increased effect of acetylcholine was studied on 15 strips in four experimental groups treated as follows:

Group-1 strips were subjected to M.E.C. acetylcholine, then washed, and after stabilization were stimulated first with M.E.C. eserine and then with M.E.C. acetylcholine. The first test of each strip thus served as a control, since it established the responsivity of the strip to M.E.C. acetylcholine alone, thus making possible the detection of any increase in the sensitized response, in the second test, over that to acetylcholine alone or to the eserine allowed to act alone at first in the second half of the experiment.

Group-2 strips were first tested with sub-M.E.C. acetylcholine (1:2,000,000), then washed and given M.E.C. eserine followed by 1:2,000,000 acetylcholine.

Group-3 preparations received M.E.C. acetylcholine, then were tested under 1:2,000,000 eserine followed by M.E.C. acetylcholine.

Group-4 experiments were made with 1:2,000,000 acetylcholine in the first part; and with 1:2,000,000 eserine, followed by 1:2,000,000 acetylcholine, given after washing.

The results are tabulated in table 3, with sample curves from the extreme groups (1 and 4) given in graphs *G* and *H* of figure 1. The group-1 experiments reveal that a contraction exceeding that to either drug alone in M.E.C. is given to their combination. In group 2, M.E.C. eserine increased the effect of weak acetylcholine greatly, and the combined effect was greater than that of the eserine alone. The group-3 tests showed that weak eserine increases the action of M.E.C. acetylcholine, the combined effect being greater than that of either drug alone in three strips out of four. In the two group-4 experiments, weak dosages of both drugs had combined effects greater than the total of their single effects.

Thus, with the solitary exception of strip no. 11, all strips responded to these various combinations of the two drugs by greater contractions than those given to either of the combined stimuli acting singly. In 11 strips out of 15, the combined effect is even greater than the sum

of the two single effects. The greatest enhancement is shown in strip no. 4, where the sensitized contraction was nearly eight times as extensive as the contraction to the more effective of the drugs acting singly, and was nearly six times the sum of the amplitudes produced by the single drugs. Acetylcholine-eserine in this particular case, than the first response to acetylcholine) but with the addition of acetylcholine bringing on a still further contraction of the twitchlike character mentioned above.

In graph *H* is shown a sample experiment (strip no. 15) in which both drugs were used in low concentrations and with

TABLE 3

SENSITIZED RESPONSE OF SPHINCTER TO ACETYLCHOLINE AND ESERINE

	Strip	Load, mg.	Amplitude of contraction, scale units				
			First test, Acetylcholine alone (=*a*)	Second test, after washing; Eserine, then Acetylcholine		Combined effect (=*b*+*c*)	Extent of augmentation (=*b*+*c*−the greater of *a* and *b*)
				(=*b*)	(=*c*)		
Group 1 MEC Acetylcholine and MEC Eserine	1	20	0.55	0.60	0.35	0.95	0.35
	2	20	1.95	1.25	1.20	2.45	0.50
	3*	20	2.10	2.85	0.75	3.60	0.75
	4	140	0.15	0.05	1.10	1.15	1.00
	5	140	0.20	0.15	0.45	0.60	0.40
	6	140	0.20	0.10	0.25	0.35	0.15
Group 2 1:2,000,000 Acetylcholine and MEC Eserine	7	20	0.15	0.40	0.65	1.05	0.65
	8	20	0.05	0.20	0.55	0.75	0.55
	9	20	0.00	0.20	0.20	0.40	0.20
Group 3 MEC Acetylcholine and 1:2,000,000 Eserine	10	20	0.60	0.00	1.00	1.00	0.40
	11	20	2.05	1.05	0.80	1.85	−0.20
	12	140	0.35	0.20	0.55	0.75	0.40
	13	140	0.30	0.40	0.45	0.85	0.45
Group 4 1:2,000,000 Acetylcholine and 1:2,000,000 Eserine	14	20	0.20	1.00	0.50	1.50	0.50
	15†	140	0.20	0.65	1.10	1.75	1.10

* Shown in Graph *G*, Fig. 1.
† Shown in Graph *H*, Fig. 1.

sensitization is thus decidedly of the "augmentative" type.

Though the generalizations in the foregoing paragraph apply equally well to all four groups of experiments, the actual tracings of the strips naturally showed differences. The extremes of drug concentrations are represented by graphs *G* and *H* in figure 1. Graph *G* shows behavior, under a low load, to M.E.C. concentrations. The solid tracing shows the effect of acetylcholine. After washing, the dotted tracing was obtained, with a marked contraction to eserine (greater, a high load, in order to develop something nearer to the maximal work capacity of the muscle. In the first test (solid tracing) the contraction was of low amplitude. The muscle was being really taxed, as evidenced by its inability to maintain the contraction, and by the fact that the second application of acetylcholine—this time in M.E.C. strength—could evoke no greater contraction. After washing, 1:2,000,000 eserine was applied. Now, after the small resultant contraction, the administration of 1:2,000,000 acetylcholine produced a contraction

much greater than that to either drug alone.

Mode of response to acetylcholine and eserine. The character of the response of the sphincter strip to these drugs deserves a little elaboration. Under either drug alone, under low loads, there is generally an initial contraction with a somewhat rounded peak due to a gradual relaxation after maximal shortening. Secondary, even tertiary, contractions of smaller amplitude may occur—the entire tracing giving something of the appearance of damped oscillations. The final state of length attained is somewhere between the starting length and that at peak shortening.

The typical reaction to the combined drugs is very different, of twitchlike character, with a more slender and sharper peak owing to the rapidity of contraction and the immediate onset of an equally rapid relaxation, which generally returns the strip to its initial length. This twitch response was obtained in 20 experiments out of 25—and was present in less well-marked degree in the other five. On the other hand, such a reaction was seen only once in 80 experiments with eserine alone, and was noted only twice in 83 experiments with acetylcholine used singly. Experiments with high loads exaggerate the contrast between the two types of response. Under the single drugs, only a small amplitude is reached and this is developed slowly, whereas the combined drugs still evoke a vigorous twitch which may go far off the scale of the recording device.

It should be mentioned that the responsivity of a particular strip can be very different toward the two drugs. The strip may react to 1:50,000 acetylcholine, and not to eserine. Only rarely was the reverse seen—a contraction to eserine and none to acetylcholine. But, it is interesting to note, sensitization still takes place in such cases, as can be seen in strips nos. 9 and 10 in table 3. Even when, as occasionally, the strip contracts to neither drug in the concentrations tried, it will still react to their combination. The muscle is affected even by the drug which fails to contract it, and its response is a "set" for the reception of the other drug.

Effect of reversed order of application. When acetylcholine is applied first, then eserine, the typical sensitized "twitch" contraction is not seen. Instead one obtains a tracing with only rounded peaks, like that shown in graph *J*, figure 1. The second contraction is of gentle character, and another application of eserine elicits only another contraction of the same sort, though occasionally of even greater amplitude.

The mechanism of the acetylcholine-eserine effect. Eserine is generally assumed to facilitate the action of acetylcholine by destroying the cholinesterase which would otherwise hydrolyze the latter drug. This supposed action of eserine is best illustrated by its promotion of the effect of small doses of acetylcholine. It is rather difficult to see why maximally effective concentrations of acetylcholine should also be made supereffective by eserine. Nor is it readily seen, in terms of the theory, why the mere removal of an interference with acetylcholine should bring about a contraction of a new type, exceeding in work output that to a maximally effective dosage of acetylcholine, or eserine, alone. Two of our findings, particularly, need to be borne in mind:

1. When eserine is given, then acetylcholine, a twitchlike contraction occurs; but a second application of acetylcholine produces only an ordinary contraction.

2. When acetylcholine is given, then eserine, only smooth contractions occur.

Both of these seem to point to the possibility that eserine modifies the mode of action of acetylcholine, but leaves un-

changed the mechanism immediately responsible for the performance of external (that is, mechanical) work. It appears not unlikely that it is the rate of influx, into the muscle cells, of the first traces of acetylcholine which determines the extent of contraction. If this influx proceeds at ordinary speed, being retarded by the presence of cholinesterase, we see the familiar round-peaked contraction. If the effect of eserine is to permit the entrance of acetylcholine to be very rapid, we can imagine that the drug briskly attacks the muscle element "all over," and can see why the muscle should respond with a "twitch," so reminiscent of the reaction of a skeletal muscle, though of course in "slow motion."

The first of the two items above is particularly favorable to this assumption of the importance of a steep gradient in the effective concentration of acetylcholine just within the reacting system. The first application of acetylcholine is the only effective one. A second application no longer encounters virgin territory and, while it may increase the difference in concentration outside and inside the reacting system, it cannot revive the steep gradient at the entrance-point. The effect of reversed order of application is in sympathy with this idea, for when acetylcholine had been given and some of it had already entered the muscle, the addition of eserine could not produce a gradient of the same steepness as in the obverse situation.

Clark (1926) has suggested that a reversible monomolecular reaction takes place between acetylcholine and some substance in the cell or on its surface. In his experiments there appeared to be no direct relationship of the amount of drug entering the cells to the amount of action produced. Here, too, lies some suggestion that it is not the absolute amount of drug which is important.

Comparison with cocaine-adrenaline sensitization. Rosenblueth (1932) has used a suggestion made by A. V. Hill to explain the action of adrenaline in the following way: Adrenin (A) combines chemically with some substance (H) in the muscle. The contraction is proportional to the amount of AH formed. Working with the heart, the nictitating membrane, blood pressure, and the nongravid cat uterus, Rosenblueth found that neither cocaine nor denervation modified the usual course of action of adrenaline.

Roepke (1937) does not believe in the implication of this hypothesis—namely, that with concentrations of the drug which yield nearly maximal responses, essentially all of the receptor substance is combined with the drug. But we feel that our results with the dilator under cocaine-adrenaline support Rosenblueth's hypothesis. The relay-race effect can best be explained either by assuming a receptor substance which, due to cocaine, becomes largely combined with adrenaline even in the case of small concentrations (as if M.E.C. adrenaline were present); or, by assuming that both cocaine and adrenaline combine with a single receptor substance of limited capacity—a situation analogous to the sequestration of a moiety of hemoglobin by carbon monoxide, leaving less of the receptor available for combination with oxygen.

Incidentally, there is a danger in assuming, from the character of the response, that only one of two synergic drugs is actually a stimulus to the immediate mechanism of contraction. When we note that the tracing of a contraction to cocaine plus adrenaline has the same shape as one to adrenaline alone, we may be tempted to speak of this as an "adrenaline type" of contraction, and to assume that the adrenaline is the only "working" member of the synergic combination. It will be shown in a following paper that

this particular response is a "dilator type" of contraction, and is not at all specific for the drug which evokes it.

Aside from the mechanism of acetylcholine-eserine action suggested above, there is of course a possibility that eserine involves itself in the chemico-physical machinery of shortening; but any test of this possibility is beyond our scope at present. We can only suggest that if eserine can produce shortening over a distinctly different route from the chain of events set off by acetylcholine, then perhaps eserine can tap sources of intracellular energy which are not available to the "physiological" mechanism through which acetylcholine works. Perhaps eserine only brings about an increased efficiency of the contracting mechanism set off by acetylcholine. But in any case, it is clear that in "augmentative" sensitization there stands revealed the fact that neither of the drugs involved—even if one of them is a normal neurohumor—acting singly can call into a kinetic condition all of the contractional energy latent within the muscle. This situation is vastly different from that which obtains in "threshold" sensitization as exemplified by the cocaine-adrenaline system. There, no more of the latent contractional energy is developed than is put to work by a high dosage of adrenaline alone.

Therapeutic advantages of the two types of sensitization. The great practical value of "threshold" sensitization inheres in the fact that one can reduce the amount of a drug which, in M.E.C., might produce unwanted effects here and there in the body, especially over long periods. But the effect producible is not greater.

Where "augmentative" sensitization occurs, one not only has this same opportunity to get the same effect with less drug, but can also obtain a greater effect than with the primary drug (or either, when neither can be recognized as "primary") alone. A further advantage in this situation is that the range of resistance over which the muscle can be made to "try" is increased, whereas in threshold sensitization—by definition—it cannot be increased, and may even be found to have *decreased,* as in the sensitization to adrenaline by cocaine.

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NOTES, CASES, INSTRUMENTS

PAROXYSMAL LACRIMATION DURING EATING FOLLOWING RECOVERY FROM FACIAL PARALYSIS

Syndrome of crocodile tears

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Lacrimation, or hypersecretion of tears, may follow irritation of the conjunctiva or cornea by dust, cold, gases, wind, or foreign body. It accompanies many inflammatory conditions of the eye and irritation of the retina by strong light. Emotional distress, frustration, and conditions associated with glandular dysfunction, as the menopause and hyperthyroidism, are common causes of lacrimation. Inflammation and irritation of the nasal mucous membrane, and stimulation of the olfactory sense by strong odors may produce sudden tearing. In addition to these de Schweinitz adds heterophoria, ametropia, tabes, and neurasthenia to the list of causes of lacrimation.

Epiphora or abnormal overflow of tears is caused by obstruction to any part of the lacrimal apparatus, from the puncta to the opening of the nasolacrimal duct in the nose.

Less common are the paroxysms of lacrimation during eating following apparent recovery from Bell's palsy, the so-called syndrome of the crocodile tears. This condition is to be differentiated from the tearing seen in the early stages of facial paralysis due to the paralysis of the orbicularis-oculi muscle, with relaxation of the lower lid and eversion of the punctum of the tear duct.

Bell's palsy or paralysis of the peripheral portion of the facial nerve may result from pathological processes located anywhere from the facial nucleus to the peripheral distribution of the nerve. By far the most frequent cause of Bell's palsy occurs at or near its exit from the stylomastoid foramen. In this area it is strangely exposed to the effects of cold and drafts, producing a thermal or pressure neuritis. Traumatic and inflammatory lesions play a lesser role in this region.

Constitutionally, diabetes, syphilis, multiple neuritis, and diphtheria may be etiological factors in peripheral facial paralysis.

Tumarkin[1] states that incomplete recovery after Bell's palsy occurs in about 20 percent of cases; of the incomplete recoveries 80 percent show crocodile tears to a greater or less degree. The syndrome consists of troublesome and annoying unilateral lacrimation while eating. The condition is interesting in connection with abnormal facial movements following injury to the facial nerve.

The causation is presumed to be a deviation of the regenerating axons from their normal course. Fibers intended for the submaxillary gland are diverted to the lacrimal gland, so that salivary stimulation produces a flow of tears. The axons which innervated the orbicularis oculi may, upon regeneration, become misdirected to supply other facial muscles. This may produce abnormal associated movements, such as closing the eye automatically draws up the corner of the mouth. As cited by Fowler,[2] experimental facial paralysis tends to show that the associated movements and the ticlike movements after recovery from traumatic or toxic injuries to the facial nerve are caused by the splitting of axons in the neuroma that form at the site of injury. There is an innervation of several parts of the face by neurofibrils from a single axon. Experimental work on degeneration and regeneration of peripheral nerves

demonstrates that regenerating fibers do not always follow the same path as before injury.

Other authorities contend the cause for these abnormalities is central-physiological or histological changes in the facial medullary nucleus or lesions of the motor cortex.

The facial nerve contains motor, sensory, and sympathetic afferent and efferent fibers. The motor root supplies, chiefly, the musculature of the face and scalp. The sympathetic efferent fibers are presumed to arise in small cells adjacent to the facial nucleus. The preganglionic fibers are distributed via the chorda tympani and greater superficial petrosal nerves to the submaxillary and sphenopalatine ganglion, respectively. Postganglionic fibers from the submaxillary ganglion are distributed, in turn, as vasodilator fibers to the submaxillary and sublingual glands. Postganglionic fibers from the sphenopalatine ganglion are secretory and vasodilator fibers to the nose, mouth, palate, parotid, and lacrimal glands.

The sensory portion contains the fibers of taste to the anterior two thirds of the tongue, and possibly deep sensibility from the face. The sensory component arises from cells in the geniculate ganglion; the peripheral sensory branches are continued in the chorda tympani and greater superficial petrosal nerves.

The lacrimal gland is supplied with nerves from three sources: the lacrimal branch of the first division of the fifth nerve, sympathetic fibers from the cervical sympathetics via the internal carotid artery, and orbital branches from the sphenopalatine ganglion. These last-named fibers are believed to arise from the facial nerve and reach the lacrimal gland via the greater superficial petrosal nerve.

Clinically it has been found that blocking the sphenopalatine ganglion relieves excessive flow of tears, and destruction of the ganglion may result in loss of tear secretion. In the anterior approach to the Gasserian ganglion, the petrosal nerve may be injured, with a resulting diminution in tearing.

The anatomy of the greater superficial petrosal nerve is apparently not well known. Evidence[3] tends to demonstrate that it has sensory connections via its tympanic branch to the tympanic plexus, being responsible for referred pain from the peripheral distribution of the sphenopalatine nerve. Connections with the otic ganglion, where also originate postganglionic fibers from the ninth nerve for the parotid gland, may provide an alternative pathway for gustatory fibers to the anterior two thirds of the tongue, autonomic secretory fibers to the chorda tympani nerve, and sensory fibers to the auriculotemporal region.

Report of case

A 12-year-old white boy complained of troublesome lacrimation of the left eye when eating certain foods. Six months before, when diving into a swimming pool, he struck another boy's head with his lower jaw. The next morning he noticed he could not close his left eye and his face was drawn to the right side. He gradually recovered the use of his facial muscles, but a flow of tears down the left cheek when eating continued. The lacrimation did not occur at every meal and no one article of food could be depended upon to excite the flow of tears every time. Doughnuts as well as pickles produced this result.

Examination showed a well-developed, healthy boy. There was no evidence of residual facial weakness. On closing the eyes a slight twitch of the corner of the mouth on the left side was noticed. The left palpebral fissure was smaller than the right. The cranial nerves were intact.

The urine and the Wassermann test were negative. No abnormalities were noted on general physical examination. There was no defect in hearing. The lacrimal apparatus was patent. The boy detected salt, sugar, and bitter substances with ease on each side of the anterior portion of the tongue. With some difficulty he demonstrated the excess lacrimation on eating. The flow was apparently quite capricious, and variable in its manifestations. When present it is annoying and ofttimes embarrassing.

Comment. The site of injury to the facial nerve was evidently in the facial canal in the region of the geniculate ganglion. Upon regeneration of the nerve, fibers evidently became misdirected from the pathways they originally pursued, resulting in lacrimation on stimulation of salivation. It would have been interesting at the time of injury to localize the site of trauma, using the methods advocated by Tremble and Penfield.[4] They estimated the loss of taste and diminution of salivary and lacrimal secretion quantitatively by simple tests, which, together with a neurologic and otologic survey, establishes the precise area of injury.

The patient also showed an abnormal associated movement; namely, twitching of the corner of the mouth when he closed the left eye.

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SOCIETY PROCEEDINGS

Edited by Dr. H. Rommel Hildreth

COLORADO OPHTHALMOLOGICAL SOCIETY

November 18, 1939

Dr. Melville Black, *presiding*

Anterior-chamber cyst

Dr. Horace Weston presented the case of J. K., aged 26 years, who was struck in the left eye by a piece of steel on April 1, 1939. This produced a wedge-shaped puncture of the cornea with some rust staining. X-ray examination of the globe was negative for foreign body. In April, a small mass considered to be a cyst was seen on the iris. When examined again in November, an oval-shaped disc about 1.5 by 2 mm. in diameter was found floating freely in the aqueous. This mass was yellowish white in color and considerably lighter than the aqueous. On motion of the eye the mass rapidly assumed the highest point, becoming hidden by the limbus when the eye was directed down. The eye was free from inflammation and the vision was 20/20. There were no subjective symptoms from its presence.

Discussion. Dr. Brobeck recalled that he had previously presented a very similar case before the society and that the appearance of the floating mass had not changed in several years.

Angiomatosis retinae

Dr. Horace Weston presented the case of J. T., a 10-year-old boy, because of striking changes in the fundus of the right eye. Ophthalmoscopic examination showed a number of yellowish-white, glistening, sharply circumscribed patches, mostly in the upper temporal region and involving the macula. The vessels were markedly tortuous in this area and some showed saccular dilatations. There were several small angiomata with arterial and venous connections. The corrected vision of the eye was 20/100. The left eye was normal. Dr. Weston stated that Dr. Arthur J. Bedell had seen the patient in consultation and had advised against X-ray or radium therapy.

Angiomatosis retinae

Dr. John C. Long presented the case of J. G., aged six years, as possibly one of von Hippel's disease. This boy showed an elevated white mass in the macular area and also grayish-white, sharply circumscribed patches in the temporal retina of the left eye. The retina in the extreme upper temporal periphery was somewhat pale in color, resembling a flat detachment. The vessels were engorged and tortuous in this area. There appeared to be several small angiomata in connection with the vessels but their extreme peripheral location made exact observation difficult. Vision was reduced to the detection of hand movements. The right eye was normal. Dr. Long stated that during the three months the mass had been observed there apparently had been some increase in the white area of retina.

Retinal detachment with recurrence following surgery

Dr. Leonard Swigert presented the case of R. B., aged 20 years, who had developed a disinsertion of the retina. This disinsertion had occurred spontaneously in an eye with one diopter of myopia. On September 1, 1939, a diathermy operation was performed, with the use of Walker pins and the Lacarrère electrode. When examined a week later the retina was in good position but there was a thrombosis of the inferior retinal vein surrounded

by extensive hemorrhages. A fibrous band developed in the hemorrhagic area which apparently was the cause of a recurrence of the detachment one month following the surgery. The macular area first became detached, and later the inferior temporal quadrant. In addition to the above-mentioned band, there was excessive proliferation in the retina around the areas treated by diathermy.

Discussion. Dr. Melville Black warned of the ever-present danger of sarcoma of the choroid in retinal detachment and urged careful ophthalmoscopic study and transillumination.

Dr. George Stine stated that this case showed two small tears that were not closed. The dense exudate in the macula and the marked retinal proliferation in the treated areas made him suspicious of a Coats's disease.

Streptothrix infection of canaliculus

Dr. William Bane demonstrated the Streptothrix organism in a slide obtained from a canaliculus of a 13-year-old child. A painless swelling was seen in the region of the canaliculus. There was no inflammatory reaction, and fluid could be syringed through the duct into the nose. A considerable amount of foreign material consisting of the Streptothrix was curetted from the passage. Prompt recovery resulted.

Discussion. Dr. Maurice Marcove stated that syringing with potassium-iodide solution will effect a cure in two or three days in such cases.

Optic-nerve complications of internal-carotid aneurysms

Dr. Rudolph Jaeger, by invitation, gave a paper on this subject. Included in his paper was a report of two cases of fusiform aneurysm of the internal carotid, one in a woman 36 years of age and the other in a man of 26 years. In both cases the optic nerve had been pushed up and anteriorly by the aneurysm so that it was pinched against the upper rim of the optic foramen. Dr. Jaeger had operated in both cases, removing the roof of the optic canal, allowing the nerve to be pushed up without pinching against bone. In both cases the internal-carotid artery was approximately four times the normal size and showed large calcified plaques in the wall. Dr. Jaeger stated that the risk of operations in this area was not great and urged prompt exploration in cases of retrobulbar nerve involvement of obscure etiology.

John C. Long,
Secretary.

MINNESOTA ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

Section on ophthalmology

November 10, 1939

Dr. Hendrie W. Grant, *president*

Recurring vitreous hemorrhages following Gonin's operation

Dr. Charles N. Spratt, Minneapolis, presented a report on this subject which was published in the July, 1940, issue of this Journal.

Discussion. Dr. Frank E. Burch, St. Paul, said he had never seen a case of recurrent hemorrhage after Gonin's operation. Reports of recurrent hemorrhage after Gonin's operation were apparently much more common when the procedure first came into general use about 10 years ago. It was one reason why we abandoned ignipuncture in favor of other methods.

Some ophthalmic surgeons with whom he has discussed the matter state that they prefer not to have the retina flat

after a period of recumbency, because they feel that one avoids injury to the retina and the formation of new holes by having it separated from the choroid by fluid at the time of operation. In any event, it is not improbable that if micropunctures penetrate the sclera, they are quickly cooled when subretinal fluid is contacted. He has frequently seen small hemorrhages in the vicinity of micropunctures but none that have penetrated into the vitreous. The technique we have tried to develop now includes the use of very short electrodes that will not penetrate deeply through the sclera. An exception is made when we are ready to make the final puncture for drainage of subretinal fluid. The Lacarrère instrument and one developed by the late Dr. John Wheeler have adjustable points, and we prefer these to the Walker pins. Thus we aim not to make punctures far enough through the sclera to touch deep tissues or permit drainage of subretinal fluid until diathermy is completed. Some operators are very enthusiastic about surface diathermy and some employ the thermophore, but the majority probably employ the micropuncture method.

Avoidance of complications is very largely dependent upon increasing refinements in instruments and technique, so that we are now having fewer complications.

Dr. W. L. Benedict, Rochester, stated that at the last meeting of the College of Surgeons there was held a symposium on detachment of the retina in which he participated. He had for that occasion looked up the records in his department. Beginning in 1926 we performed 17 operations on 15 patients by the Gonin method and at the end of one year after operation had to list all of them as failures. (Some of them were operated upon by himself, some by Dr. Lillie, some by Dr. Bair.) We used the electric cautery, to which there is an objection, as Dr. Burch has mentioned, the tip becoming cool when it comes in contact with fluids of the eye. We did not resort to Paquelin's cautery—first, because we did not have one; and second, because we thought it too cumbersome. What cases we considered as successful operations, for the purpose of the symposium, were appraised at nine months. With reports from five different institutions, all showed that less than 50 percent of the operations for detachment by all methods were successful. In our own group, we use as the criterion of success three requirements: 1. There must be no further diminution of vision. 2. Visual fields must be better than before operation. 3. There must be anatomical replacement of the retina. Judged on the basis of these three points, successes after nine months varied from 25 percent to 45 percent in various institutions. Now, the cause of failures in Gonin's operation were attributed largely to trauma and the tremendous reaction. He has not in mind any of the details of the other cases in which operation was by the Gonin method, but he does know there was considerable reaction following some of the operations. Many times the vitreous would be so cloudy it would be impossible to make out the place of puncture, to know if the retina had become reattached. Three patients had a satisfactory functional result which lasted less than three months.

Carcinoma of lacrimal duct

Dr. Charles N. Spratt said that in 1936 he reported a case of primary cancer of the lacrimal sac, the second in American literature. He recently had another case of this kind. A man, aged 66 years, stated that some five years previously there had appeared a swelling over the lacrimal sac. This gradually increased in size and the eye was pushed forward

and outward. Examination disclosed a hard mass over the left lacrimal sac extending into the lower lid and above in the nasal portion of the orbital cavity. Vision sufficed only to count fingers at six feet. The entire contents of the orbit were removed by separating the periosteum on the upper and temporal portions and everting the mass. As the last portion gave way the lacrimal bone with the sac was removed. This mass had extended into the antrum, which was lined by thickened membrane.

Dr. Verhoeff has examined sections and his report is "a papillary epidermoid carcinoma of the antrum. Section of the sac shows an extremely malignant carcinoma invading and infiltrating the muscles." Penman and Wolff have reported a case of malignant papilloma of the sac and have collected 64 cases of malignant tumors of the sac, 24 of which were classed as carcinoma. Recently McCool of San Francisco reported a malignant tumor which is probably a carcinoma primary in the lacrimal sac. So far as he has been able to determine the case shown is the fourth in American literature.

Discussion. Dr. Frank Burch said that during the past 13 years at the University Hospital and in private work he has seen but one case of malignancy of the lacrimal sac which could be considered as distinctly primary in the sac. This very malignant case resulted in extensive infiltration into the orbit, ultimately requiring extenteration. He does not know how one can distinguish the origin of malignancy in this vicinity; that is, whether it begins in the sac or in the nasal lacrimal duct, as in this case. Tumors of the lacrimal sac are relatively rare, although Dr. Lane has collected and published a considerable series of reported cases. To make a diagnosis of tumor originating from the lacrimal duct must be quite difficult.

Dr. W. L. Benedict had seen only one patient who had carcinoma of the nasal duct that he suspected was primary in the duct. This patient was referred to us in 1936 by a chiropractor, and was first seen by Dr. New and Dr. Figi. Dr. Benedict obtained a biopsy through a trochar. The patient refused operation. Two years later he received a letter from an oculist near the patient's home, telling him she thought a paste had been applied and she had suffered great mutilation. He has no further details of this particular patient. He has seen carcinoma appearing in the region of the nasal duct but believed the tumor was not primary in the duct.

George E. McGeary,
Secretary.

SAINT LOUIS OPHTHALMIC SOCIETY

November 16, 1939

Dr. B. Y. Alvis, *president*

Short-wave diathermy in ophthalmology

Dr. Daniel Bisno presented a paper on this subject.

Discussion. Dr. William Meinberg said that during the past six or eight months it had been his pleasure to observe and follow many of these cases at the County Hospital. The cases used in this study were invariably those that did not respond to the usual methods of treatment. He believed that if this selectivity had not been the rule, a larger percentage of good results would have been obtained.

In regard to the contraindications and complications, he said short-wave diathermy is a form of deep heat, and it is obvious that a burn of the eye or orbit by this type of heat would be quite serious. The therapeutic dose is usually the greatest amount of heat that a given

patient can comfortably tolerate. Thus, the intensity of the heat is governed by the patient's reaction to it. For this reason short-wave diathermy cannot be used on small children and only with great caution in conditions presenting trigeminal-nerve involvement. It was interesting to note that the same patient could not tolerate the same amount of heat each day. This was perhaps caused by a daily variation of the line voltage to the machine.

The results in glaucoma were quite discouraging. A woman of about 60 years of age was admitted to the hospital because of a broken hip. She also had a furunculosis of the chest, head, and eyelids. In response to the interne's request for an eye consultation, we found the right eye had been lost four years ago following an operation for glaucoma. The tension in the left eye was 77 mm. (Schiötz). Pilocarpine, eserine locally, and hypertonic solutions intravenously were of no avail. Attempts to lower the tension with short-wave diathermy were equally unsuccessful. The tension was finally reduced by the combined use of mecholyl and prostigmine.

Dr. W. M. James said the application of heat locally causes an increase in the blood supply to the eye and probably facilitates the exchange of substances between the blood and the intraocular fluids. Heat, cold, massage, and paracentesis all have a similar effect. Massage and paracentesis are more effective than a local application of either heat or cold in producing a local hyperemia.

Dr. Bisno in conclusion said that when we first obtained the machine we thought we would cure everything. We treated glaucoma, tubercular iritis, kerato-iritis, and vitreous hemorrhage and obtained varying results. Answering Dr. Lange about loss of heat sensation, one might have to test the patient's sensation to heat with a warm test tube. If they have a good heat sensation then one might go ahead. The vitreous temperature can be raised to 110°F. and above. In answer to Dr. James, regarding the intraocular effect of heat, there was no change noted in the caliber of the retinal vessels after use of short-wave diathermy.

Recent advances in corneal transplant

Dr. Meyer Wiener presented a communication on this subject which was published in this Journal (Aug., 1940).

Discussion. Dr. B. Y. Alvis said he would like to state he had seen several patients that Dr. McKinney had operated on by the Castroviejo method. He reported 21 cases done by that method and gave the results. The visual acuity of the best one was 6/15, the worst one 6/60. The cornea looked like a clear window. The transplant becomes a little bit milky and then clears up and remains clear. Dr. McKinney stated the graft remained clear in these cases from the beginning. The surface of the cornea looks smooth and there is no thickening at the edge. He believes corneal transplantation is coming to the fore. Another point of interest is the presence or absence of considerable areas of clear cornea. If there is clear cornea next to the graft it supplies nourishment to the transplanted graft. The remaining portion of the cornea becomes clearer after a successful transplant.

Dr. William M. James said the punch presented by Dr. Wiener certainly cuts a beveled circle of corneal tissue. Whether the distortion and strain of stretching the corneal tissue over the bullet nose of the punch will interfere with the subsequent viability and transparency of the graft must be determined.

Dr. Meyer Wiener in answer to the question as to whether to perform a resection or a transplant said he once took

Dr. Castroviejo's course on transplantation and discussed his cases with him. In his opinion, a majority of cases would have done as well or better with a resection than with a transplant, the resection being much safer. He had a patient, with resulting vision of 6/15 in one eye, who had had light perception in each eye. He took the poorer eye and performed a resection and that man was able to drive a car through traffic and read fine print. He believes most transplants do become milky for a few days. Some have been reported clear from the day of the operation.

He believes that optical iridectomy should be tried before anything else if the cornea is clear. The ideal optical iridectomy is not the iridectomy performed by the average ophthalmologist. He thinks it is most important to get the smallest iris opening possible.

As to the advantage of using living or dead cornea, he cannot answer. Most men have followed the recommendation of Filatov who finds the cornea from dead people gives him better results than the cornea transplanted from a freshly enucleated eye. He also finds it is better after it has been refrigerated a few days rather than when transplanted immediately. Everyone agrees that the tissue must not be traumatized. Best results anyone has obtained are by Thomas of England. This punch does exactly what scissors do and produces no more crushing or bruising of the tissues.

Untoward reaction following use of mecholyl and prostigmine

Dr. Theodore E. Sanders presented a case report on this subject.

Discussion. Dr. William M. James reported on the work done by Dr. Lee Cady and himself in the clinic on optic-nerve atrophy. Mecholyl was used by instillation and injection. They had no systemic effect from it. It was used on patients averaging 40 years of age and above. They did not find any beneficial results in luetic optic-nerve atrophy with it.

Dr. J. D. Calhoun had occasion to try mecholyl in one case in an acute attack of glaucoma. The tension was 55 mm. Hg when first seen. The cornea was steamy, vision down to counting fingers at two feet. Within an hour after the use of mecholyl, using a drop every 10 minutes and six instillations, the vision came up to 6/15 and the tension dropped to 14 mm. There was no systemic reaction. The patient was a woman of about 50 years of age in good physical condition. He then gave her 2-percent pilocarpine to use at home. The tension stayed down to 12 mm. the first day, then 14 mm. and 16 mm. on the fifth day following the single use of mecholyl. He has cut the pilocarpine down to 1 percent. Her fields show a 5-degree contraction. There is no cupping of the disc.

Adolph C. Lange,
Editor.

CHICAGO OPHTHALMOLOGICAL SOCIETY

November 20, 1939

Dr. Earle B. Fowler, *president*

Conjunctivo-glandular syndrome of Parinaud

Dr. Carl Apple presented a man, aged 32 years, first seen on October 23, 1939, with a history of swelling of the right upper lid and in the preauricular and right maxillary region of two weeks' duration. The conjunctival surface of the right upper lid was markedly inflamed and granular, and at the center of the retrotarsal fold was a 3 by 3-mm. vegetative yellowish area. The right preauricular and submaxillary glands were greatly swollen and tender, and the patient com-

plained of severe pain, especially at night. The temperature ranged from 98.2°F. to 99.0°F. The glands became larger during the first 10 days of observation and one of the upper cervical glands also became involved. The condition of the eye and the glands has shown some improvement.

The blood Wassermann test was negative. Differential blood count showed 6-percent eosinophilia but was otherwise normal; urinalysis was negative. This man has been treated with argyrol, local applications, antiseptics, and potassium iodide by mouth. Sulfanilamide was tried for three days early in the course, but the condition apparently became worse.

The only growth obtained from cultured smears was gram-negative pliomorphic bacilli with gram-positive granules. Smears for acid-fast bacilli were negative. Agglutination test for tularemia was negative. Intraperitoneal injection of curretted material into a guinea pig on October 30th has so far produced no result. Pathologic studies will be made at the end of six weeks.

A section of conjunctival tissue was excised and sent to Dr. Sanford Gifford for special staining by Verhoeff's method.

Dr. Gifford has suggested that the following tests be made: (a) agglutination test for tularemia; (b) examination of excised tissue fixed in Zenker's fluid and stained by Verhoeff's method; (c) examination of excised or curretted material for acid-fast bacilli; (d) guinea-pig inoculation; (e) a careful inquiry regarding exposure to wild rabbits or squirrels, or the presence of cats in the house; and (f) cultures of aspirated pus on serum or agar under a 10-percent CO_2 tension.

The patient stated that there is a Persian cat in his home. All the suggested tests have been carried out, and although a report has not yet been received of the biopsy and histologic studies, it is felt that this case belongs in the group of Leptothricosis conjunctivae.

Boeck's sarcoid of palpebral conjunctiva

Dr. Martha Rubin Folk said that F. M., a white man, aged 49 years, presented himself at the clinic on August 7, 1939. He complained of gradual development of redness of the right eye for the past six months without any pain or discharge. The appearance of this eye has not changed to date. The history states that 20 years ago cervical glands became swollen and enlarged gradually, without suppuration or pain. After eight months they were removed at Cook County Hospital. (The hospital was unable to furnish a report of the pathologic condition as the record had been lost.) On July 9, 1928, he was readmitted to Cook County Hospital where a diagnosis of peptic ulcer was made. Under Sippy treatment he recovered and was discharged within four days. Since that time he has had no other symptoms.

Findings: O.S., normal; O.D., vision was 0.5—with correction, 1.0. There was slight narrowing of palpebral fissure; the lid margins were red and thickened; the palpebral conjunctiva beefy red and hyperplastic. Rounded outgrowths of granulation tissue were found springing from the palpebral conjunctiva near the fornices. The bulbar conjunctiva was moderately injected, with symblepharon on both sides of the cornea, about 3 mm. from the limbus. The cornea was clear, the iris gray, the pupil reacted to light and accommodaton; the disc and tactile tension were normal; the fundus showed no pathologic condition of the retinal vessels. Conjunctival cultures and smears showed large gram-positive rod diphtheroids and a few diplococci, and Staphylococcus albus. Smears for acid-fast bacilli were negative. Direct smears of the pa-

tient's conjunctiva to rabbit eyes produced no inflammation after 48 hours. Pure culture of diphtheroids injected subconjunctivally into the rabbit's eye produced no inflammation in 48 hours. The physical examination showed nothing of significance. The diagnosis was confirmed by histologic examination of a biopsy.

The patient has received the following treatment: large doses of iodides for several weeks (on the supposition that it might be a blastomycosis); sulfanilamide for four days without any effect; dental treatment for pyorrhea; diphtheroid autogenous vaccine; low-voltage X ray (two treatments to date).

Hypotony after contusion

Dr. Peter C. Kronfeld presented the case of a man, aged 65 years, who sustained a severe contusion of the left eye 11 years ago. On August 1, 1939, examination revealed an essentially normal right eye. In the left eye the lens was completely opaque and the tension below the range of the Schiötz tonometer. An uncomplicated cataract extraction was performed on August 1, 1939, followed by a moderately severe postoperative reaction. The hypotony has persisted. The eyeground is fairly visible. The disc shows a swelling of four diopters of the type seen in choked disc. This swelling is the characteristic finding in hypotonic eyes. The remainder of the eyeground is not clearly visible. The lower half of the retina, however, appears to be detached. The retina is perfectly transparent there, but the vessels are darker and more tortuous. The patient's central vision now permits finger counting at one-half meter, not improved by lenses. Perimetry shows a defect occupying the upper half and including the point of fixation. Gonioscopic examination shows the chamber angle to be normal except for a few peripheral anterior adhesions related to the cataract extraction. The presence of a traumatc cyclodialysis can be excluded. The assumption of a retinal detachment with tear appears to be the most probable explanation of the permanent hypotony.

Bilateral duane's syndrome

Dr. Erwin E. Grossman presented a five-year-old boy, first seen in the outpatient department. The mother stated that the boy had some difficulty in looking to either side, but there was no head tilting nor diplopia. This condition had been present since birth. There was no history of a similar condition in other members of the family. There was no history of injury or illness except whooping cough.

Upon examination there were no visible evidences of congenital defect. External examination of the eyes was entirely negative; there was no facial paralysis. The corneae were clear, the pupils were equal in size, shape, and outline, and reacted well to light and accommodation. The eyegrounds were normal. The refractive error was corrected with a $+1.50$ D.sph. $\bigcirc$ $+.50$ D.cyl. ax. 90° in each eye, with resultant vision of 20/20.

Examination of the extraocular muscles revealed the following: In the primary position the eyes appeared to be in good alignment. When looking to either side the abductor eye did not move beyond the midline. There was a noticeable retraction of the globe upon adduction, which measured 2.5 mm. with the exophthalmometer, and also a decrease in the size of the palpebral fissure to the extent of 2 mm. There was also a marked degree of oblique motion in the adducting eye, rotating up and in. There was a definite deficiency in convergence, especially marked in the right eye. The degree of adduction appeared to be normal.

This case illustrates nearly all the

points of Duane's original description: (1) deficiency in abduction; (2) retraction of the globe and decrease in size of the palpebral fissure, upon adduction; (3) weakness of convergence; (4) oblique motion of the adducting eye; (5) the congenital nature of the condition.

Although cases of Duane's syndrome are quite common, the number of reported cases of the bilateral type are quite few. Nearly a third of the reported cases showed an associated seventh-nerve involvement, which was never present in any of the unilateral cases, and was not present in this case.

Detachment of the zonular lamella of the anterior lens capsule in a foundry worker

Dr. M. S. Osherwitz presented M. W., a 68-year-old white man who had been employed in a zinc plant for 40 years. His work necessitated his looking into a large zinc-melting furnace from which he withdrew molten zinc. Fifteen years ago he had a cataract removed from his left eye. About one year ago vision in his right eye began to fail.

Upon examination both corneae showed several maculae. The left eye was aphakic, with an iridectomy from his previous cataract operation. Tension and fundi were normal. In the lens of the right eye there was a spokelike opacification of both anterior and posterior cortices, not the characteristic central sharply demarcated posterior subcapsular opacification of thermal cataract. On the anterior surface of the lens in its central portion there was a fine clear transparent pelliclelike membrane detached from the lens except for one fixed extremity which faded imperceptibly into the lens. The free lateral borders of the membrane were curled or rolled toward each other to form a tubelike structure.

That this type of detachment may follow long exposure to high degrees of heat has long been recognized. It has been known to occur in glass-blowers and foundry workers. The first report in the American literature of such a case was given by Dr. S. J. Meyers in the Archives of Ophthalmology, 1928, volume 57, page 121.

The incidence and distribution of trachoma in the United States

Dr. Harry S. Gradle discussed the geographic incidence of trachoma in the United States and presented a map giving the distribution. This could not be considered as strictly accurate, inasmuch as trachoma is not uniformly reportable in the various states. In the trachoma clinics of Southern Illinois, 3,350 cases have been discovered within the past five years, but from adjacent areas the cases reported have been comparatively few. On that basis it is estimated that the number of cases reported to the United States Public Health Service represents but 10 percent of the total cases in the United States. There is probably a minimum of 35,000 cases among non-Indian peoples, and 25,000 among the Indians. Of the former approximately 70 percent are to be found along the old trail made by early settlers from the Atlantic Seaboard to the junction of the Ohio and Mississippi Rivers. The remainder of the cases are scattered throughout the country. Among the Indians, 60 percent of the incidence is in the tribes of the Southwest. The type of trachoma varies enormously with the character of the populations and the degree of sanitation. The cleaner the people, the less virulent is the trachoma.

Metastatic carcinoma of choroid primary in the prostate

Dr. Max Kulvin read a paper on this

subject which was published in this Journal (August, 1940).

Discussion. Dr. William A. Mann said the relative infrequency of carcinoma of the choroid, especially cases having their origin in the prostate, makes this paper interesting. It is possible that carcinoma of the choroid may be a little more common than we think, inasmuch as it usually occurs in the terminal stages of carcinomatosis and in most instances enucleation of the eye is not indicated. Many cases may therefore occur without being reported.

In the past six years at the Veterans' Hospital, with one of the largest tumor clinics in the world, we have seen only one other case of choroidal carcinoma. This was discovered in a man with generalized carcinomatosis, the origin of which was obscure. The eye was not enucleated and no autopsy was performed. In our pathologic files at Northwestern University we have an eye from Dr. Gifford's service. The pathologic work was done by Dr. Cushman. This man had an automobile accident with injury to the chest. Following this about a month later he began to complain of loss of vision in the left eye. Tumor was diagnosed, the eye was enucleated, and the pathologic picture was that of typical carcinoma. Subsequently the man died of carcinomatosis and did not have an autopsy. The exact source was not known, but was thought to be in the stomach.

Robert von der Heydt.

AMERICAN JOURNAL OF OPHTHALMOLOGY

Published Monthly by the Ophthalmic Publishing Company

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Author's proofs should be corrected and returned within forty-eight hours to the *Manuscript Editor.* Twenty-five reprints of each article will be supplied to the author without charge. Additional reprints may be obtained from the printer, the George Banta Publishing Company, 450-458 Ahnaip Street, Menasha, Wisconsin, if ordered at the time proofs are returned. But reprints to contain colored plates must be ordered when the article is accepted.

EDITING AN OPHTHALMOLOGICAL JOURNAL

Almost 10 years ago, in April, 1931, to be exact, the present editor became editor in chief of this Journal. It now seems best for him to relinquish this pleasant task to other hands. It has been hard work but lots of fun.

The editor's connection with the American Journal of Ophthalmology commenced in 1923. In 1926 he was appointed an assistant editor in charge of society proceedings; later he took over the news and abstracting departments. In 1930, with the failure of Dr. Clarence Loeb's health it was no longer possible for him to take an active part in the management; hence the managerial office was moved to Saint Louis at that time and the present editor appointed manager, which post he has held to date. He was always fortunate in being able to find competent associate managers: Mrs. Delano, later Mrs. Johnson; Miss Lumaghi, now Mrs. Douglas; and Miss Coleman. Without such help the work would have been impossible.

In 1928 Dr. Jackson, founder of the joint publications amalgamated in 1918 under the name of the American Journal of Ophthalmology, and editor in chief for 10 years, wished to be relieved, and Dr. William H. Crisp, who had served as editor of the Year Book

* Deceased.

until that date, when it was discontinued, assumed charge. He retained office for three and a half years, at which time he desired more time for other work, and the editorship was passed on to the now retiring editor. Dr. Crisp, however, retained charge of the Abstract Department, which he had taken over at the time of his appointment. He enlarged it and has made it by far the best in the English literature.

When the present editor first took over as editor in chief, editing and managing the Journal required between 80 and 90 hours a month. Since, six months after assuming charge, there was added also his appointment as departmental chief in ophthalmology in The Washington University School of Medicine, the burden for the next two or three years was very heavy, for a private practice also had to be cared for. Fortunately at this time contact was made with the present manuscript editor, Miss Emma S. Buss, and from then the Journal work began to be easier. As she became more familiar with the routine, an ever-increasing part of the editing has been passed to her, so that it has been possible to reduce greatly the hours spent on the Journal. It is good news for the Journal that Miss Buss will continue as manuscript editor.

The present editor now feels as his predecessors in their own cases have felt, that he wants more hours for the direction of his department and for his practice. The department of ophthalmology of Washington University entered the field of graduate teaching several years ago. In each subsequent year this has become a more important feature and its direction has required more effort. General ophthalmic fields, too, have broadened in the past 10 years, and all of these require more time in the department as well as in private practice. To study a patient completely now is far different and additionally time consuming than it was 10 years ago.

What are the needed qualities for Journal leadership in these days and in this changing world? Among them certainly are a sound knowledge of ophthalmology, a flair for writing, acquaintance with the medical profession, especially with ophthalmologists and their problems, willingness to work and to see work through to its conclusion, a good educational and social background, and a knowledge of foreign languages—although this may not be so important for several years to come.

The arrangement of having the editor also manager of the Journal has served well because it enables him to keep in close touch with the business end of the publication. The disadvantages are obvious, more time is required and he has to be a business man as well as an editor. This means familiarity with and constant attention to the problems of subscriptions and advertising.

To fulfill these requirements the directors have elected Dr. Derrick Vail editor in chief, a man who, they believe, has the needed qualifications and in whose hands the Journal will continue to prosper. Ophthalmologists have always shown a remarkable interest in this materialization of Dr. Jackson's vision and will without doubt accord the new editor the splendid support that they have given Dr. Jackson and his successors. Congratulations to Dr. Vail and to the Journal on his appointment.

Lawrence T. Post.

PRESENT-DAY OPHTHALMIC LITERATURE

In answer to a question, the late Professor Mautner of Vienna is reported to have said "When I wish to read something

really worth while, I lock myself in my study and read something that I have written myself." American Ophthalmology today finds itself in much the same position. In by-gone days we were flooded with two English, five German, three French, two Italian, a variable number of Spanish, one Scandinavian, one Japanese, one Palestine, and a few Latin-American periodicals so that an earnest polyglot had no time for even the St. Eve. Post. Today, the British Journal of Ophthalmology appears with regularity and the newly regenerated Swiss Ophthalmologica holds to a somewhat irregular time schedule. So the ophthalmic reading public is almost restricted to the two American periodicals which have now assumed the dominant role in the ophthalmic literature of the world.

But should that permit us to sit back and rest? Is this not the time to join hands with the ophthalmic profession of the entire Western Hemisphere and advance the progress of Pan-American ophthalmology to a point where its supremacy can never be challenged by the Old World? We of the United States are not sufficiently acquainted with our Latin-American confrères and do not know their scientific achievements, principally because of our ignorance of their language. Their facility with English far exceeds our linguistic ability, and, in consequence, the ophthalmologists of Central and South America know far more about us than we do about them.

A start in the direction of breaking down that barrier can be made by the publication in each issue of the American Journal of Ophthalmology of the table of contents of each of the Latin-American ophthalmic publications. Inquiry among a few of the editors of the Southern Hemisphere revealed an eager desire for such an exchange which would in turn lead to a better understanding among the New World ophthalmologists. All of the papers that were presented in English at the recent Pan-American Congress of Ophthalmology have been spoken for by the various Spanish and Portuguese ophthalmic periodicals of Latin-America. It is hoped that the American journals will assume the same responsibility toward the Latin papers.

But why the urge toward Pan-Americanism where there are no diplomatic or commercial relations involved? Originally, our American ophthalmologists were trained in England, and later in Germany and Austria, until the time arrived when our own training facilities equalled and then surpassed those of Europe. Coincidentally with the training was developed the habit of using and considering as superior the foreign ophthalmic literature, and such habits are hard to break. Much the same situation pertained throughout Latin-America. But today, neither training nor literature is possible in Continental Europe and probably will not be for another quarter century, if ever. To prevent the development of insular isolation in clinical ophthalmology or in research, contact with other nations is essential. What is more natural than to turn to our neighbors of the South for a free exchange of ideas and methods, which exchange can be initiated and furthered, primarily, through ophthalmic periodicals.

Harry S. Gradle.

CROSS-CYLINDER MISCONCEPTIONS

Although refraction work permits of more mathematical precision than any other department of the practice of medicine, it is well to remember that no refractive test is at all times entirely reliable. In eyes of very regular curvature the objective tests with the retinoscope may come very close to perfection, al-

though too often the irregularities of the refractive surfaces introduce important elements of uncertainty and unreliability. As to the subjective tests at the trial case, we find many subjects in whom absolute precision is delightfully possible. But here again, whatever methods we employ, the cases in which we experience difficulty in arriving at the desired result are provokingly numerous.

To say that any given test is regarded as superior to other tests used for a like purpose is not necessarily to argue that good results cannot be obtained with those other tests, but merely that in the majority of instances the speaker has found the preferred test quicker or more reliable (or both) than other tests.

Among the human variables with which we must contend in refraction work is the tendency of examiner and examinee to have in mind different interpretations of the same phraseology. The terms "black," "dull," "dark," "bright," and "clear" may frequently mean one thing to the physician and another to his patient. It is a mistake to employ an excessively limited vocabulary for examination purposes, and it is often well to present the same question to the patient in several different forms.

Friedman, whose discussion of the teaching of refraction was referred to in these columns recently (September, page 1056), has since published a "critique" whose purpose is stated to be an examination of the uses of the cross cylinder (Archives of Ophthalmology, volume 24, page 490). This second paper seems to reveal on the one hand a fundamental misconception as to the nature of the cross-cylinder tests, and on the other hand an excessive fixity of language in questioning the patient as to the appearances produced by the different positions of the cross cylinder.

It is of the very essence of the cross-cylinder tests that any cross-cylinder combination, in any of the standard positions before the patient's eye, leaves the average of the lens measurement in the various meridians entirely unchanged. Whether we are using the 0.12, 0.25, 0.50, or 1.00 D. cross cylinder (total cylindrical strength of 0.25, 0.50, 1.00, or 2.00 D.), the average strength of the lens combination before the eye, in all meridians, remains the same; since in the two principal meridians the plus is averaged with an equal minus, the mathematical result being zero.

In the opinion of the present writer, the action of the cross-cylinder tests is, as a rule, most reliably utilized when the lenses already in the trial frame are of such total plus or minus effect as to leave the accommodation approximately relaxed, without appreciable fogging; rather than with the patient's vision fogged, as recommended by Friedman. With successive changes in cylinder, the sphere in the trial frame is also to be modified from time to time to maintain this general condition of relaxed accommodation without fogging.

Too generally, especially in the presence of active accommodation, it is the custom to ask the patient to tell which position of the cross cylinder blurs least or most; the examiner accepting uncritically the answers thus obtained, without attempting to analyze the possibility of misunderstanding on the part of the patient. Not infrequently, closer questioning will reveal that with the position which the patient declares to produce most blur he can actually read more letters than with the opposite and supposedly clearer position. This possibility of error due to a loose form of questioning becomes greater as we approach the point at which the final measurement is arrived at, the point at which the differences to be disclosed are small and the patient finds

greater difficulty in making any choice whatever. To accept at this stage the mere statement that there is more or less blur, or greater or less clarity, one way than the other is often to fail in obtaining a sharply accurate measurement of the patient's astigmatism.

The only safe way to eliminate this source of error is to conduct the final stages of the examination with very critical insistence upon indication by the patient as to whether, on the very lowest line then more or less legible, he can actually read more letters with one position of the cross cylinder than the other. He will often answer such a question intelligently without reading the letters aloud; although in case of doubt it will be advisable to demand such actual reading.

The fact—referred to in Friedman's essay and often insisted upon in the course of teaching by the present writer—that the cross-cylinder test for strength may tend to be somewhat unreliable when the astigmatic axis is vertical or horizontal becomes of much less significance if this critical mode of questioning is applied in the final stages, and conversely of much greater significance if simple questions as to blur or clarity are employed throughout. There is certainly no reason to believe, as Friedman suggests, that the cross-cylinder test for strength is any more liable to this defect than tests with simple plus or minus cylinders. It may also be noted, in opposition to a statement by Friedman, that this liability to inaccuracy, as to the vertical and horizontal positions, applies just as greatly to astigmatism against the rule as to direct astigmatism. In other words, the patient is just as likely to overstate the former as to understate the latter.

Friedman's unqualified remark that the test letters are more legible when their vertical components are clear and their horizontal components blurred can hardly be applied to the Snellen type in which all lines of the letters are of equal width. The real point to bear in mind in this relation is that the line of letters often looks brighter (not necessarily being more legible) to the patient under the conditions referred to.

Friedman and others have introduced into the terminology of refraction what seems to the present writer to be an unnecessary complication, by speaking of "building up the spherocylindric combination" as though this were a separate element of the measurement of refraction, apart from measurement of the sphere or of the cylinder as such. Surely, in every measurement of refractive error at the trial case, we must devote our attention at one moment to the sphere, at another to astigmatic strength, and at another to astigmatic axis, returning always from any one of these to consideration of the others until we are satisfied that the whole measurement has been whittled down to the utmost possible exactitude. The phrase "building up the spherocylindric combination" represents an epitome of the whole measurement of refractive errors, and not merely a particular part of the procedure.

Without any corresponding advantages, the use by Friedman and others of simple cylinders in place of the cross cylinder, as applied to either strength or axis, misses the whole point of the cross-cylinder principle, namely the zero of average change in the use of the patient's accommodation, and the opportunity thus afforded for discovering whether one position or other of the cross cylinder renders legible a greater number of letters than the other position.

Friedman says with partial truth that "in determining cylinder strength the criterion of improved visual acuity seems more reliable than the comparative blurs

involved in the cross-cylinder test." If he will proceed to apply the cross-cylinder tests with concentration upon comparative visual acuity in the contrasted positions, instead of merely inquiring how much blur the patient experiences, he will probably learn to view the cross-cylinder tests with much more cordial approval than that indicated in his recent essays.

W. H. Crisp.

BOOK NOTICE

THE HUMAN RETINA AND ENTOPTIC PHENOMENA. By E. P. Fortin. 207 pages, 124 illustrations in black and white, three in colors. Printed in French by A. Frascoli and A. Bindi, Buenos Aires, 1938.

This monograph is a rather long and rambling rediscussion of material in papers published since 1903 in Paris and Buenos Aires on the histology of the human retina and entoptic phenomena. The author's contribution to the normal structure of the human retina consists of a confirmation of much that has been reported by other writers and a few points of difference from what is commonly accepted. The numerous illustrations are, as a rule, only fair photomicrographs. Fortin has been an important contributor to our knowledge of the living retina from entoptic phenomena. At the end of the work, there is appended a list of the 70 publications of the author on these as well as other topics in ophthalmology.

Harvey D. Lamb.

CORRESPONDENCE

THE NORM OF BLOOD URIC ACID

September 12, 1940.

Dr. H. C. Kluever,
Fort Dodge, Iowa.
Dear Dr. Kluever:

I was much interested in your article on hyperuricemia. There is one statement in it which is a little confusing to me and I thought you might help to clear it up. This is your reference to the blood uric acid as "4.1 to 5.6 mg. as against the normal of 1 to 3 mg. per 100 c.c." It is the normal figure which bothers me. I have had blood uric acid run on several patients and most of them have run between 3 and 4 mg. In our Passavant Memorial Hospital laboratory 2 to 4 mg. is considered normal. They calculate it on the basis of whole blood, using the Folin direct method. I would be interested in the method you used in your tests and your authority for the normal figure. It did look to me as if the uric acid must be a factor and perhaps the only factor in your cases but the amounts were all somewhat above 4 mg. I thought perhaps a little note to the Journal might save other ophthalmologists some confusion about this. There may be a number of cases in which amounts between 3 and 4 mg. are a factor and I think we all ought to keep an eye out for them.

With best regards, I am
Sincerely yours,
(Signed) Sanford R. Gifford, M.D.

September 21, 1940.

Doctor Sanford R. Gifford,
Chicago, Illinois.
Dear Doctor Gifford:

I wish to thank you for your letter concerning blood uric-acid concentrations. The values of 1 to 3 mg. of uric acid per 100 c.c. of blood as originally found by Folin and Denis were given as normal in my article first because differences of opinion still existed as to what the normal figure might be, and second because examinations of blood for hyperuricemia are made too infrequently by ophthalmologists without in addition limiting reëxaminations by following the higher normal values. It seemed well that

we start with a low figure and include a greater number of cases and do more frequent reëxaminations of questionable cases. If an eye inflammation responds to a reduction of blood uric-acid concentration, the possibility of uric acid being a factor must be carefully considered; if it does not respond we must remember that Peters and Van Slyke consider as normal, even concentrations as high as 5 mg. and state that "no pathological significance can be attached to a single observation that does not exceed 6 mg. and perhaps 7 mg." I have enclosed a list of authors who give normal values ranging from 1 to 5 mg. Naturally if we were to pay no attention to a concentration as high as 5 mg. none of the cases which I reported could have been studied. Our method of determination is Benedict's method, using a Folin stable standard and the Folin-Wu filtrate.

I extend my kindest regards.

Sincerely yours,

(Signed) H. C. Kluever, M.D.

1 and 2 to 3 and 3½ mg.
Gradwold. Clinical laboratory methods and diagnosis. Saint Louis, The C. B. Mosby Company, 1935, p. 150.

Normal 2 to 3½ mg.
Hawk and Bergeim. Practical physiological chemistry. Philadelphia, P. Blakiston's Son and Company, 1926, p. 378.

1½ to 4 mg.
Myers. Piersol's Cyclopedia of medicine. Philadelphia, F. A. Davis Company, 1935, v. 6, p. 447.

2 to 4 mg.
Todd and Sanford. Clinical diagnosis. Ed. 9, Philadelphia, W. B. Saunders Company, 1939, p. 349.

2 to 4 mg.
Kolmer and Boerner. Approved laboratory technique. New York, D. Appleton-Century Company, 1938, p. 712.

2 to 4 mg.
Cantarow and Trumper. Clinical biochemistry. Philadelphia, W. B. Saunders Company, 1939, p. 120.

2½ to 5 mg.
Peters and Van Slyke. Quantitative clinical chemistry. Baltimore, Williams and Wilkins Company, 1932, pp. 421-422.

Priority in the field of gonioscopy

To the editor of the American Journal of Ophthalmology:

Dear Dr. Post:

In the August number of the American Journal of Ophthalmology appeared an interesting article by Dr. H. S. Sugar, entitled "Concerning the chamber angle. 1. Gonioscopy."

Although well written and presenting new facts, there are some statements concerning the history of gonioscopy and the development of the methods of examination of the angle, which, in the interest of justice and fairness, I should like to rectify.

The first observer to make extensive use of the binocular corneal microscope in gonioscopy, and publish his findings, was Dr. Sigurd Werner[1] (1932). Dr. Thornburn,[2] in 1927, also mentioned having used it occasionally. Dr. Bruce[3] published in 1933 an article in which he reported that he and Dr. Castroviejo had used the corneal microscope for the localization of foreign bodies in the angle. Dr. Otto Barkan[4] (1936) constructed a floor stand and a hanging device by which the handling of the microscope could be made easier, avoiding the trouble of keeping the heavy, cumbersome instrument in both hands to focus it. Similar stands have been devised later by Drs. Hartshorne, Bogart, MacLean, and others.

The term "microgonioscopy," coined by Dr. Barkan, has not in my opinion any significance, as the corneal microscope is more often used with a magnification of ×10 to ×15, which is the same as that given by my instrument the gonioscope. The difference between both methods of examination of the angle is that with the gonioscope the observation is indirectly made through a redressing prism, while with the corneal microscope a direct lateral view is obtained.

My purpose in using the prism was to allow the observer to stand always in front of the patient, without having to move around to observe the four cardinal sides of the angle.

Referring to posterior synechiae as the cause of glaucoma, Dr. Sugar says on page 859: "Since then (the papers of Knies and Weber) Thorburn, Werner, Troncoso, and Barkan have shown that instead of their (the peripheral synechiae) being the cause of glaucoma, they are probably a relatively late result." Since my first article on gonioscopy[5] (1925), and before the publication of the papers of Thornburn and others, I had already pointed out that synechiae are not the cause, but the result of the glaucomatous process. By accurate statistics, I proved later (1935) that the angle may be opened even after mild attacks of congestive glaucoma and in simple glaucoma even with high tension.

Although questions of priority are usually of little importance in science, still it is only fair to give due credit to whom it belongs.

Very sincerely yours,

(Signed)

Manuel Uribe Troncoso, M.D.

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[1] S. Werner. Gonioskopische Untersuchungen bei Glaucoma primarium. Acta Ophth., 1932, v. 10, p. 427.

[2] A. Thorburn. A gonioscopic study of anterior peripheral synechia in primary glaucoma. Thesis, Stockholm, 1927.

[3] G. M. Bruce. Vizualization of foreign bodies in the iridocorneal angle. Arch. of Ophth., 1933, v. 10, p. 615.

[4] O. Barkan. On the genesis of glaucoma. An improved method based on slitlamp microscopy of the angle. Amer. Jour. Ophth., 1936, v. 19, p. 209.

[5] M. Uribe Troncoso. Gonioscopy and its clinical applications. Amer. Jour. Ophth., 1925, v. 8, p. 433.

ABSTRACT DEPARTMENT

EDITED BY DR. WILLIAM H. CRISP

ASSISTED BY DR. GEORGE A. FILMER

Abstracts are classified under the divisions listed below, which broadly correspond to those formerly used in the Ophthalmic Year Book. It must be remembered that any given paper may belong to several divisions of ophthalmology, although here it is mentioned only in one. Not all of the headings will necessarily be found in any one issue of the Journal.

CLASSIFICATION

1. General methods of diagnosis
2. Therapeutics and operations
3. Physiologic optics, refraction, and color vision
4. Ocular movements
5. Conjunctiva
6. Cornea and sclera
7. Uveal tract, sympathetic disease, and aqueous humor
8. Glaucoma and ocular tension
9. Crystalline lens
10. Retina and vitreous
11. Optic nerve and toxic amblyopias
12. Visual tracts and centers
13. Eyeball and orbit
14. Eyelids and lacrimal apparatus
15. Tumors
16. Injuries
17. Systemic diseases and parasites
18. Hygiene, sociology, education, and history
19. Anatomy, embryology, and comparative ophthalmology.

1

GENERAL METHODS OF DIAGNOSIS

Bair, H. L. **Some fundamental physiologic principles in study of the visual field.** Arch. of Ophth., 1940, v. 24, July, pp. 10-20.

Study of the visual field is divided into two fundamental divisions: topographic, which deals with the shape and extent of field defects, and quantitative, which considers the degree of the loss of perception in the area as compared to normal sensibility. Each division may be subdivided into achromatic and chromatic. The author finds that upon using larger test stimuli and lower levels of adaptational background brightness, study of the visual field is more reliable in the presence of uncorrected ametropia and refractional aberrations. A new principle, depending on the use of a selected low level of adaptational background brightness, is presented. The author feels that this method is more delicate and accurate than that ordinarily used at relatively high levels of light adaptation and minimizes certain technical difficulties. Some mistaken beliefs regarding the detection of field defects with chromatic stimuli are explained according to the normal physiology of color perception throughout the field, especially the fairly steep gradients of color sensibility and the reversal of the gradient for perception of blue on approaching the center of the field, and the prevalence of partial color blindness.

J. Hewitt Judd.

Bouman, H. D. **Electrical excitability of the eye. A study in clinical physiology.** Ophthalmologica, 1940, v. 99, May, p. 394.

The author discusses problems arising when the eye is electrically stimulated. Electrical excitation is due to stimulation of the optic nerve. This fact is of value in differentiating loss of vision due to destruction of the retina from that caused by nerve changes.

F. Herbert Haessler.

Cooper, S. N. **Perimetry abused.** Proc. All-India Ophth. Soc., 1938, v. 6, pp. 177-185.

Cooper stresses the importance of fields being charted with objects of various sizes and at various distances.

Lawrence G. Dunlap.

Danis, M. **Color photography of the fundus oculi.** Bull. Soc. Belge d'Opht., 1940, no. 79, p. 58.

The writer describes briefly his method of color photography of the fundus. He states that the problem is simplified by using Kodachrome film. (2 figures in color.)

Jerome B. Thomas.

Dekking, H. M. **Eye photography with the miniature camera.** Ophthalmologica, v. 99, May, p. 413.

The author describes a complex illuminating accessory for the miniature camera, designed to make color photography of the eye possible and convenient. The optical and physiologic difficulties are discussed.

F. Herbert Haessler.

Evans, J. N. **What is the matter with the hand ophthalmoscope?** Brooklyn Hosp. Jour., 1940, April, v. 2, pp. 80-85.

The author discusses a number of possible improvements in the design of the hand ophthalmoscope, including a "streamlined" head with improved prism and pinhole, filters, telescopic magnification, and a caliber-measuring scale. T. E. Sanders.

Evans, J. N. **The reflecting retinoscope.** Amer. Jour. Ophth., 1940, v. 23, Oct., pp. 1159-1160.

Friedman, Benjamin. **A screen for ophthalmoscopic examination.** Arch. of Ophth., 1940, v. 24, Aug., pp. 373.

A disc of black bakelite 8.25 cm. in diameter is attached to the back of any standard ophthalmoscope head by means of a spring clip. This may be pivoted and fixed in any position desired, thus forming a barrier between the nose and mouth of the patient and those of the oculist. It is readily detachable, light, and inexpensive, and may be sterilized in almost any antiseptic solution. J. Hewitt Judd.

Gifford, H. **Use of fluorescein intravenously as an aid to ophthalmic diagnosis and treatment.** Arch. of Ophth., 1940, v. 24, July, pp. 122-131.

The intravenous injection of a 10-percent solution of sodium fluorescein is recommended as a method of studying the circulation o the aqueous in clinical cases. It has been found to be nontoxic and not unpleasant to the patient. Its time of appearance and concentration in the aqueous depend chiefly on the state of the capillary permeability in the iris and ciliary body. The volume flow of blood, the concentration of blood protein, the size of the anterior chamber, and the viscosity of the aqueous appear to be minor factors. The time of appearance of the dye in the aqueous in normal eyes, which is easily demonstrated, averages about three minutes. This test may prove valuable in establishing the diagnosis of early keratoconus since the time of appearance and the concentration of the dye are definitely diminished in this condition. Treatment with parasympathetic-stimulating drugs is therefore indicated. The procedure is a definite aid in proving the presence and position of vitreous in the anterior chamber, and has proved definitely valuable in selecting the site of a filtering operation for glaucoma following cataract extraction. In the clinical study

of the problem of glaucoma, it may prove valuable in separating the secretory from the purely obstructive type. The application of this test to general medicine has not yet been investigated but there is a possibility of using it in vascular disorders in which capillary permeability is a factor as in migraine, malignant hypertension, and toxemia of pregnancy. J. Hewitt Judd.

Gradle, H. S., and Sugar, H. S. **Concerning the chamber angle. 3. A clinical method of goniometry.** Amer. Jour. Ophth., 1940, v. 23, Oct., pp. 1135-1139.

Kleefeld, G. **Illumination of the slit-lamp by krypton globes. (For examination of the eye with polarizing filters.)** Bull. Soc. Belge d'Opht., 1940, no. 79, p. 145.

Owing to the replacement of the inert gas argon by krypton in these globes, their brilliance has been greatly increased without reduction of length of life. Jerome B. Thomas.

Nano, H. M. **Telegradimeter for campimetry.** La Semana Med., 1940, v. 47, Aug. 22, pp. 441-443.

An optical projector carries a slide by means of which are projected on to the Bjerrum screen a series of black points, thirty degrees apart circumferentially and five degrees apart radially, and also two ovals in the zones corresponding to the blind spots. W. H. Crisp.

Sloan, L. L. **Instruments and techniques for clinical testing of light sense. 4. Size of pupil as a variable factor in the determination of the light minimum.** Arch. of Ophth., 1940, v. 24, Aug., pp. 258-275. (See Section 3, Physiologic optics, refraction, and color vision.)

Traquair, H. M. **Perimetry and the visual pathway.** Glasgow Med. Jour., 1940, v. 133, April, pp. 105-118. (See Section 16, Injuries.)

2

THERAPEUTICS AND OPERATIONS

Alvaro, M. E. **Progress in ocular therapeutics.** Rev. Oto-Neuro-Oft., 1939, v. 14, June, p. 142.

Staphylococcus toxin, vitamin therapy, irradiation, goniotomy, hormone therapy, the use of the sulphonamide group of drugs, heparin in central venous thrombosis, diathermy, and paredrine in refraction are among the newer developments mentioned by the author. Edward P. Burch.

Battignani, Agostino. **Greifswalder stain in ophthalmology.** Boll. d'Ocul., 1939, v. 18, Oct., pp. 811-824.

Colonies of staphylococcus aureus, colon bacillus, streptococcus, and pneumococcus were incubated in agar to which Greifswalder stain had been added. No microörganism developed if the 0.5-percent solution was used but the 0.25-percent solution allowed the streptococcus and the pneumococcus to grow. Ulcers of the cornea and conjunctiva and simple conjunctivitis were provoked in rabbit eyes by infecting such structures with the above bacteria. Under treatment with the Greifswalder stain the inflammatory symptoms disappeared within two weeks while the pneumococcus infection recovered in three weeks. Clinical reports show that treatment with the mixture gave brilliant results in patients affected by subacute Morax-Axenfeld conjunctivitis, in a patient with acute catarrhal conjunctivitis from streptococcus, and in a case of second-stage trachoma. Recovery took place and organisms disappeared in the course of a few days. (Bibliography.) M. Lombardo.

Chhatre, E. V. **Prontosil in ophthalmology.** Proc. All-India Ophth. Soc., 1938, v. 6, pp. 186-193.

Since prontosil liberates sulphanilamide in the blood and tissues, the author used it most satisfactorily in cases of orbital cellulitis, conjunctivitis, dacryocystitis, and lid abscess. He cautions that the blood picture must be carefully watched. Cyanosis is due to the formation of sulphemoglobin and occasionally methemoglobin. The latter is relieved by discontinuing the drug and administering oxygen.

Lawrence G. Dunlap.

Doherty, W. B. **Olivary-tipped anterior-chamber needle.** Amer. Jour. Ophth., 1940, v. 23, Oct., p. 1161.

Focosi, M. **The behavior of blood pressure during some ocular surgical procedures. Advantages and action of blood-letting. Pathogenesis of some operative complications.** Boll. d'Ocul., 1939, v. 18, Sept., pp. 689-728.

Blood-pressure changes during operation for cataract (109 cases) and glaucoma (52 cases) are given in tabulated form. The blood pressure increased during the late stages of the operation and became higher the older the patient. Increase in blood pressure was absent or slight in patients who had been subjected to blood-letting. In these cases the incidence of vitreous loss or expulsive hemorrhage in cataract or detachment of the choroid in glaucoma was decreased. The blood-letting was performed 12 hours before the operation and the amount of blood removed was from 400 to 500 c.c. (Bibliography.)

M. Lombardo.

Gundersen, Trygve. **Convalescent blood for treatment of herpes zoster ophthalmicus.** Arch. of Ophth., 1940, v. 24, July, pp. 132-141.

This report, based on the study of 12 additional cases, confirms the author's previous conclusions (Amer. Jour. Ophth., 1936, v. 19, p. 934) regarding the value of the serum. Of the entire series of patients, now totalling 22, who have received herpes-zoster convalescent blood and the final outcome of whose condition is known, eighteen retained useful vision (6/18 or better in the affected eye) and four lost useful vision. Three cases in which treatment had no apparent effect are reported in detail. All had severe and well-established ocular infection before treatment was instituted. The author concludes that if between 250 and 450 c.c. of blood is given before ocular infection is well established, good results may be expected. J. Hewitt Judd.

Guyton, J. S. **Effects of sulphanilamide and sulfapyridine on the Koch-Weeks bacillus (hemophilus influenzae).** Arch. of Ophth., 1940, v. 23, June, pp. 1243-1251.

The author presents a summary of the literature and the results of experiments, showing that both sulphanilamide and sulfapyridine produce an inhibitory or bactericidal effect on the growth of this organism in blood broth The effect was more marked on the encapsulated "mucoid" strain than on the nonencapsulated "smooth" strain. Sulfapyridine, in therapeutic doses, exerts a much greater effect than does sulphanilamide. However, in concentrations of 59 mg. per 100 c.c. sulphanilamide appears to be more effective than sulfapyridine. The oral administration of sulphanilamide to two patients and of sulfapyridine to one patient with ocular infections due to this bacillus

produced significant therapeutic effects. The local treatment of three patients with an ointment containing 5-percent sulphanilamide produced no significant beneficial effects. J. Hewitt Judd.

Heath, P., and Sachs, E. **Antagonism between adrenergic drugs and atropine in the isolated iris dilator.** Arch. of Ophth., 1940, v. 24, July, pp. 142-148.

This is part of a series of studies in which isolated radial strips of the iris dilator of albino rabbits were contracted by epinephrine and neosynephrin in physiologic doses and then other drugs applied, noting synergism or antagonism. It was found that the application of atropine relaxed the contracted dilator. The amount of the effect was dependent upon the relative concentration of the antagonistic drugs.

J. Hewitt Judd.

Hilding, A. C. **Removal of sclerocorneal sutures.** Arch. of Ophth., 1940, v. 24, Aug., pp. 371-372.

The author describes his procedure for removal of sutures so as to avoid any injury of the eye should the patient suddenly roll his eyes upward while the suture is being held. Of chief importance is a vertical position of the scissors so that the suture will not catch on the blade.

J. Hewitt Judd.

Parker, F. C. **A serrated discission needle.** Arch. of Ophth., 1940, v. 24, Aug., pp. 372-373.

The needle described has a point adapted for easy puncture and serrations which begin 2 mm. from the point and extend the length of the blade. The shaft is of uniform diameter throughout so as to slide through freely, yet snugly fill the wound opening.

J. Hewitt Judd.

Pfeiffer, Raymond L. **A pressure dressing.** Amer. Jour. Ophth., 1940, Oct., pp. 1156-1158.

Powell, L. S., and Smith, H. S. **Studies of the visual fields in connection with tryparsamide therapy.** Arch. of Ophth., 1940, v. 24, Aug., pp. 276-280.

The authors review the literature and report the results of visual-field studies on three nonsyphilitic and 13 syphilitic patients given tryparsamide intravenously. Constriction of the visual field occurred in 11, three showed no appreciable change, and five showed an early expansion of the field followed by a constriction. Since the visual fields show early toxic manifestations of the drug, the authors urge that this method be used as a reliable method of control for tryparsamide therapy.

J. Hewitt Judd.

Van Lint, A. **Iritis during treatment of a case of chronic blennorrhea with sulphamide and vaccine.** Bull. Soc. Belge d'Opht., 1940, no. 79, p. 150. (See Section 7, Uveal tract, sympathetic disease, and aqueous humor.)

3

PHYSIOLOGIC OPTICS, REFRACTION, AND COLOR VISION

Bartley, S. H., and Bishop, G. H. **Optic-nerve response to retinal stimulation in the rabbit.** Proc. Soc. Exper. Biol. and Med., 1940, v. 44, May, p. 39.

This is a rather technical article. The authors conclude that the retinal activity arises in elements distal to the ganglion-cell layer, and probably in the sense cells. Records obtained with and without a diffusing screen were so closely similar as to indicate that the responses observed following projection of a small bright image on the retina were chiefly due to stray light,

illuminating the retina as a whole by internal dispersion from the image.

Ralph W. Danielson.

Batt, J. C. **Mirror-writing in normal adults.** Jour. Mental Science, 1940, v. 86, July, p. 680.

Batt noted the fact that most cases of mirror-writing were discussed in conjunction with some pathologic lesion or some possible mental deficiency. He felt, therefore, that it would be well to examine some normal people for evidence of this condition. One hundred people were thus examined, mostly hospital employees. The frequency and causation of the condition are discussed, and in the light of present knowledge the etiology is accounted for by the balance between visual and kinesthetic elements under the guiding influence of the dominant cerebral hemisphere. However, there are still some points not fully explained. (5 references.)

Ralph W. Danielson.

Colenbrander, M. D. **On the measurement of the power of the lens and the accommodation.** Ophthalmologica, 1940, v. 99, May, p. 402.

The author points out that by means of a monochromatic source of light, one can exactly measure the chromatic aberration of the eye, and get reliable values for the chromatic aberration of the lens. Assuming that the specific chromatic aberration is alike in all human eyes, it is possible to measure the refractive power of the lens and the axial length of the eyeball. The accommodation was measured with a new test chart, and no relationship between refractive strength of the lens and accommodation was found.

F. Herbert Haessler.

Craik, K. J. W. **Transmission of light by the eye media.** Jour. of Physiology, 1940, v. 98, May, p. 179.

Stiles and Crawford discovered in 1933 that subjective brightness is not proportional to pupil area in man. By traversing a small pencil of light across the pupil, they measured the actual effectiveness of the different parts of the pupil in contributing to the total subjective brightness, and found that light entering the eye near the margin of the pupil is only about one quarter as effective as that entering through the central part. They conclude that this effect is probably not due to greater light absorption by the marginal part of the lens, but to variations in the directional sensitivity of the retina. That the phenomenon originates in the retina and not in the eye media is rendered probable by the fact that the effect is absent with low-intensity light of 430 to 435 millimicrons falling on the dark-adapted parafovea. It seemed desirable to test this hypothesis by direct measurement of the transmission by the central and marginal parts of the lens and cornea in isolated eyes. Stiles and Crawford's explanation of the effect, in terms of directional sensitivity of the retina, is corroborated by direct measurement of the relative light transmission at the margin and center of the lens in the excised eyes of the cat. Persistent irregular variations in transmission up to 10 degrees and a steady decline at the extreme margin were found, but the curve is totally different from that obtained by subjective investigation in man, the discrepancy being often as much as 50 degrees. (3 references.)

Ralph W. Danielson.

Ferree, C. E., and Rand, G. **A more nearly absolute method of testing and**

rating vision. Arch. of Ophth., 1940, v. 24, Aug., pp. 292-315.

The comparative merits of the capital-letter charts and the doubly-broken-circle chart are presented and a new method of rating vision in terms of power to discriminate detail in the four principal meridians of the eye—horizontal, vertical, and the two oblique—is described. In the capital-letter charts the multiple test objects are entirely too variable and irregular as to form, gross or overall size, and size of the details to allow consistent and reproducible results. The doubly-broken-circle chart was devised to correct the deficiencies of the capital-letter type chart. It is discussed under the following headings: test objects, the test chart and method of using it, the report of the testee, and the rating scale on auxiliary advantages. The authors claim that with it vision can be rated in a correctly graded scale and when it is used with proper control of illumination and the other variable factors, high reproducibility and consistency of results can be obtained from time to time and from place to place.

J. Hewitt Judd.

Lijo Pavia, J. **The so-called "schools of vision"; their dangers.** Rev. Oto-Neuro-Oft., 1939, v. 14, June, p. 137.

A diatribe against the treatment of myopia without glasses after the method of the "Bates School."

Edward P. Burch.

Ludvigh, Elek. **Determination and significance of the photopic retinal visibility curve.** Arch. of Ophth., 1940, v. 24, July, pp. 168-181.

By applying suitable corrections for the absorption and reflection of light by the ocular media of the human eye a photopic ocular visibility curve is transformed into a photopic retinal visibility curve. The photopic retinal visibility curve is markedly symmetric, and the data are well represented by a simple probability function. No photosensitive substance so far found in animal eyes has been shown to possess an absorption spectrum corresponding to the photopic retinal visibility curve. The symmetry and smoothness of this curve suggest that it is due to the operation of either a single process or a large number of processes rather than to the operation of three or four processes. Various possible explanations of the shape of the photopic retinal visibility curve are considered.

J. Hewitt Judd.

Morgan, O. G. **Some cases of traumatic myopia.** Brit. Jour. Ophth., 1940, v. 24, Aug., pp. 403-406. (See Section 16, Injuries.)

Pascal, J. I. **A self-setting cross cylinder.** Amer. Jour. Ophth., 1940, v. 23, Sept., pp. 1039-1040.

Petronio, G. **Behavior of the light-stimulus threshold and the field of vision in fatigued subjects.** Arch. di Ottal., 1940, v. 47, Jan.-Feb., p. 19.

The author investigated the behavior of the light stimulus and the field of vision in healthy subjects fatigued by means of a rowing apparatus. He came to the conclusion that after fatigue there is a lowering of the light stimulus and a reduction in the size of the field of vision. The theory offered for these modifications is based on circulation, p_H of the blood, metabolism, and reaction of the neurovegetative system.

H. D. Scarney.

Sloan, L. L. **Instruments and techniques for clinical testing of light sense.**

4. Size of pupil as a variable factor in the determination of the light minimum. Arch. of Ophth., 1940, v. 24, Aug., pp. 258-275.

Measurements of the light minimum or threshold of the dark-adapted eye are influenced by the size of the subject's pupil. Experimental determinations of the threshold for a series of different sizes of pupil show that, within the accuracy of the measurements, the product of threshold multiplied by area of pupil is a constant. It is therefore possible to reduce all threshold measurements made with different sizes of pupil to a comparable basis if the diameter of the entrance pupil is known. A camera and auxiliary apparatus for photographing the pupil in the dark are described.

J. Hewitt Judd.

Verhoeff, F. H. **Phi phenomenon and anomalous projection.** Arch. of Ophth., 1940, v. 24, Aug., pp. 247-251.

The Phi phenomenon can be elicited by alternate stimulation of the two foveas of squinters with good visual acuity in each eye, who are manifesting anomalous projection. In the case of a person with convergent squint, who without binocular fixation is projecting his foveal images to the "crossing point" of his eyes, Phi movement of the images is greatly reduced or completely abolished. These observations accord with the fact that both eyes, and particularly the two foveas, are habitually employed simultaneously by squinters who are free from amblyopia. In the case of a squinter conditions can be produced so that with alternate stimulation of the same two contraocular retinal areas the direction of Phi movement when the subject is squinting is opposite to that when he is fixating binocularly. In its present form, Wertheimer's explanation of the Phi phenomenon is highly improbable. The physiologic mechanism responsible for the contraocular Phi involves cortical points which do not bear fixed functional relation to the retinas.

J. Hewitt Judd.

Wenaas, E. J., Evans, W. H., and Odom, R. E. **A study of practical cycloplegia; with special reference to the use of paredrine.** Amer. Jour. Ophth., 1940, v. 23, Oct., pp. 1123-1135.

4

OCULAR MOVEMENTS

Casten, V. G. **Isolated congenital absence of the inferior rectus muscle.** Arch. of Ophth., 1940, v. 24, July, pp. 55-61.

The literature is briefly reviewed and two cases are presented in detail, with photographs showing the eyes in the various cardinal positions. The author concludes that congenital paralysis of the inferior rectus muscle cannot be differentiated clinically from congenital absence of the muscle without operative investigation. Congenital hypertropia resulting from absence of the inferior rectus muscle can be greatly improved by advancing and transplanting the external rectus muscle to a point midway between the normal position of the external and inferior rectus muscles. If the hypertropia is excessive, tenotomy of the inferior oblique muscle should be combined with transplantation and advancement of the external rectus muscle. The transplanted external rectus muscle then has two additional actions, extorsion and depression, both functions of the normal inferior rectus muscle.

J. Hewitt Judd.

Cogan, D. G. **Waltzing guinea pigs with particular reference to ocular movements and righting reflexes.** Arch. of Ophth., 1940, v. 24, July, pp. 78-82.

Waltzing guinea pigs show a characteristic and complete absence of labyrinthine control over ocular movements and position of the eyes; over movements and position of the head; and over the righting reflexes when tested by rotation, the Barany test, and tilting for skew deviation. Although labyrinthine control is absent in the waltzing guinea pig, the righting reflex is carried out with more or less success by the visual sense and by contact with the ground. These two criteria can be separately studied by allowing the animal to fall through the air, with and without a blindfold, and land on a flat surface. The righting in the air is for the waltzer a function of vision; the righting on a flat surface is in the case of the blindfolded waltzer a function of contact. J. Hewitt Judd.

Ford, F. R., and Walsh, F. B. **Tonic deviations of eyes produced by movements of head; with special reference to otolith reflexes.** Arch. of Ophth., 1940, v. 23, June, pp. 1274-1284.

After discussing volitional movements of the eyes; optic-fixation reflexes; labyrinthine reflexes, both from the semicircular canals and from the otoliths; tonic neck reflexes; and Bell's phenomenon, two cases are reported in which deviations of the eyes were produced by movements or changes in the position of the head. In the first case there was loss of voluntary lateral gaze but the eyes might be moved laterally by active and passive movements of the head. The ocular deviations were of two types: (a) those produced by slow movements of the head, which were well sustained and were abolished if fixation was prevented, and (b) those produced by sudden, quick movements of the head, which were poorly sustained and which persisted when fixation was prevented. The first type of deviation was thought to be due to optic-fixation reflexes and the second type to reflexes arising in the semicircular canals. The second case presented the loss of volitional movements of the eyes in the vertical plane. When the head was flexed the eyes deviated upward, and when the head was extended the eyes deviated down. These deviations were well sustained and were not dependent on fixation. Slow movements were as effective as quick movements. By the use of the tilting table it was shown that these reactions were not due to tonic neck reflexes, but probably arose in the otolith organs. These observations suggest that in man as well as in experimental animals the otolith reflexes play an important role in the tonic deviations of the eyes which are associated with movements of the head. J. Hewitt Judd.

Lodge, W. O. **A bodkin for strabismus operations.** Brit. Jour. Ophth., 1940, v. 24, Aug., pp. 407.

Lodge describes in detail a miniature self-retaining strabismus hook (designed by himself) which renders the extraocular muscle accessible and puts it at rest. (Figure.)

D. F. Harbridge.

Mann, Ida. **Convergence deficiency.** Brit. Jour. Ophth., 1940, v. 24, Aug., pp. 373-390. (See Amer. Jour. Ophth., 1940, v. 23, Aug., p. 945.)

Sniderman, H. R. **External ophthalmoplegia.** Amer. Jour. Ophth., 1940, v. 23, Sept., pp. 1035-1038.

Verhage, J. W. C. **Miners' nystagmus and disturbances of adaptation.** Ophthalmologica, 1940, v. 99, May, p. 503.

The author discusses the more important theories of the etiology of miners' nystagmus. Industrial efficiency is not always reduced proportionately to the nystagmus. A systematic examination of 91 miners with nystagmus and 47 miners with normal eyes disclosed disturbances of adaptation in 70 percent of the nystagmus patients. Those who had nystagmus without subjective disturbances (eight in this series) had normal adaptation. The author concludes that it is predominantly the disturbance of adaptation and not the nystagmus which causes discomfort. The great contrasts and rapid changes of illumination in the mine are assumed to constitute the cause. F. Herbert Haessler.

8

GLAUCOMA AND OCULAR TENSION

Badot, J. **Is it necessary to operate for glaucoma?** Bull. Soc. Belge d'Opht., 1940, no. 79, p. 60.

Report of an unoperated case of glaucoma ending in rupture of the cornea. The author recommends operation in all cases of hypertension.

Jerome B. Thomas.

Casini, Francesco. **Observations and considerations in eight cases of chronic glaucoma simplex in the same family.** (Contribution to the question of heredity of glaucoma.) Arch. di Ottal., 1940, v. 47, Jan.-Feb., p. 1.

Eight cases of bilateral chronic glaucoma simplex were observed in a family during four generations. A complete study of the genealogic tree was made, showing the tendency of hereditary glaucoma in various generations, the equal distribution according to sex, and the various constitutional hereditary factors transmitted. H. D. Scarney.

Chandler, P. A. **Intradiem tension studies in chronic simple glaucoma.** Arch. of Ophth., 1940, v. 24, July, pp. 62-77.

Twenty-two cases of chronic simple glaucoma are reported with visual fields and tension curves, in which intradiem tension studies were done. The tension was taken four times daily. The period of study was from three to five days. The first day of the study no treatment was employed. On succeeding days different miotics were used and their effect on the tension was recorded. In one group of patients the tension was always found to be within normal limits and was affected little, if at all, by miotics. In a second group the tension was sometimes found to be elevated but was maintained at normal levels with some miotic. In the third group the tension was sometimes found to be elevated and was not satisfactorily controlled by miotics. In some cases the studies furnished valuable data for deciding whether or not to operate. When operation was contraindicated for general reasons, the study helped to determine the most effective miotic therapy. J. Hewitt Judd.

Cordero, Celso. **The hepatic function in glaucoma.** Arch. di Ottal., 1940, v. 47, Jan.-Feb., p. 16.

Many tests for hepatic function and blood chemistry were done on patients afflicted with chronic glaucoma simplex. As the result of the tests, definite hypofunction of the liver was shown. The author feels that in other types of glaucoma, also, there are evidences of liver hypofunction. H. D. Scarney.

Fallica, G. **Late results of antiglaucomatous operations.** Boll. d'Ocul., 1939, v. 18, Oct., pp. 780-796.

Among 3,226 cases of glaucoma operated on by Bardelli of the University of Florence, 56 were cases of acute glaucoma in which the Graefe sclero-iridectomy had been performed, 217 were of chronic glaucoma with low pathologic tension and regular anterior chamber in which the Lagrange sclero-iridectomy had been performed, and 302 were cases of chronic glaucoma with high tension and shallow chamber in which an Elliot trephining had been done. These cases were kept under observation for a period of from 2 to 20 years. The results, with special regard to central and peripheral vision and tension, are given in tabulated form. There was only a small percentage of unsuccessful results. The writer thinks that both of these two fistulization methods are effective. Late infection in these cases is due to a rupture of the bleb which is of traumatic origin in all cases. (Bibliography.)

M. Lombardo.

Friedenwald, J. S. **Perspectives in glaucoma research.** Arch. of Ophth., 1940, v. 24, July, pp. 107-121.

The author discusses the physiochemical factors in the formation of the aqueous, the chloride content of the aqueous, and the aqueous as a dialysate and as a secretion. The hypertonicity of the aqueous suggests that there may be water losses through the cornea, and the fact that the aqueous is nearly in thermodynamic equilibrium with the blood in respect to some components, and very far from equilibrium in respect to others, indicates that the blood-aqueous barrier may be structurally and functionally complex. Mechanisms of pressure control exist in the eye which are capable of compensating for changes in arterial or venous blood pressure and for changes in the protein osmotic pressure of the blood. Since this is still present in aniridia, the regulating mechanisms must exist outside of the iris. After discussing the source and outflow of the aqueous, the mechanism for its reabsorption and the mechanism of its secretion, the author concludes that there are in the eye effector mechanisms by which the rates of formation and of reabsorption are governed and that these effector mechanisms are subject to the control of the vegetative nervous system. Also, if there are neuro-effectors controlling the intraocular pressure, there are probably also neuro-receptors which respond to changes in intraocular pressure and initiate the reflexes that terminate in effector action.

J. Hewitt Judd.

Gradle, H. S., and Sugar, H. S. **Concerning the chamber angle. 2. Exfoliation of the zonular lamella and glaucoma capsulare.** Amer. Jour. Ophth., 1940, v. 23, Sept., pp. 982-997.

Halbertsma, K. T. A. **Presence of histamine in the human aqueous.** Ophthalmologica, 1940, v. 99, May, p. 443.

The aqueous of 14 patients with and without glaucoma was added to perfusion fluid. That from glaucomatous eyes caused definite vasoconstriction characteristic of histamine and histamine-like bodies; that from the non-glaucomatous eyes did not.

F. Herbert Haessler.

Shivarova, E. D. **Knapp's adrenalin reaction in the early diagnosis of glaucoma.** Viestnik Opht., 1940, v. 16, pt. 4, p. 228.

Dilatation of the pupil after instilla-

tion of adrenalin was found in 12 out of 40 subjects without clinical symptoms of glaucoma, and in 24 out of 25 glaucoma patients. A tabulation of the reaction of 39 children of glaucoma patients shows a positive reaction in 22. The author explains this by an inherited instability of the vegetative nervous system which causes a disturbance in the vasomotor-regulating apparatus of the eye. Ray K. Daily.

Sugar, H. S. **Concerning the chamber angle. 1. Gonioscopy.** Amer. Jour. Ophth., 1940, v. 23, Aug., pp. 853-866.

Tichomirov, P. E. **The significance of the Marx-Schmidt drinking test in the early diagnosis of glaucoma.** Viestnik Opht., 1940, v. 16, pts. 2-3, p. 127.

The rise in intraocular tension following the ingestion of a liter of water is one of the provocative tests for glaucoma. In a clinical study on the evaluation of the test, the author found it positive in 90 percent of the cases. A negative test is not conclusive. A rise of over 6 mm. in a normal eye signifies instability of the tension-regulating mechanism. The response to the test demonstrates the undesirable effect of a large fluid intake in glaucoma, and the advisability of restricting it.

Ray K. Daily.

Turner, H. H. **An intraocular imbalance indicative of endocrine deficiency.** Pennsylvania Med. Jour., 1940, v. 43, July, p. 1413.

The author presents three cases of glaucoma in which the chambers deepened and tension was reduced after administration of a polyglandular preparation consisting of extracts of anterior pituitary, testes, and thyroid.

T. M. Shapira.

Vogt, Alfred. **Cyclodiathermy puncture in cases of glaucoma.** Brit. Jour. Ophth., 1940, v. 24, June, pp. 288-297. (See Amer. Jour. Ophth., 1940, v. 23, May, p. 589.)

Weekers, L., and Bonhomme, F. **Operative treatment for advanced glaucoma which is menacing central vision.** Ophthalmologica, 1940, v. 99, April, p. 180; also Bull. Soc. Belge d'Opht., 1940, no. 79, p. 48.

The author believes that it is not sufficient to render the intraocular tension normal. It is better, in order to preserve vision, to bring about hypotony. Medical treatment is almost always insufficient. The most effective of all antiglaucomatous operations is iridencleisis. It reduces the tension more than any other, is less disfiguring, and is safe. Central vision is not destroyed by it, and what peripheral vision is left is preserved and sometimes increased.

F. Herbert Haessler.

Wolfe, O., and Wolfe, R. M. **The Troncoso magnesium implant and the seton operation used on the same patient.** Amer. Jour. Ophth., 1940, v. 23, Aug., pp. 920-921.

Zolotareva, M. M., and Medvedev, H. I. **Pseudoglaucoma and glaucoma without excavation.** Viestnik Opht., 1939, v. 15, pt. 6, p. 40.

A review of the 27 cases reported in the literature, and a report of four cases of chronic glaucoma without excavation and of one case of deep excavation without clinical symptoms of glaucoma. Glaucoma without excavation calls for the same treatment as glaucoma with excavation. Excavation without symptoms of glaucoma calls for very careful and thorough func-

tional examination of the eye. In the absence of any disturbance of function no treatment is indicated.

Ray K. Daily.

9

CRYSTALLINE LENS

Arndt, E. W. **Lens sliding in removal of cataracts.** Brit. Jour. Ophth., 1940, v. 24, April, pp. 182-188.

The total number of cataract cases, excluding congenital, operated upon in this manner is presented in tabular form. The preparation of the patient for operation and the method of operation are described in full. It is stated that this operation is not for beginners but that experience and a very light touch are necessary. (Figures, tables.)

D. F. Harbridge.

Beetham, W. P. **Atopic cataracts.** Arch. of Ophth., 1940, v. 24, July, pp. 21-37.

Atopy is the term applied to the occurrence of eczema, asthma and hay fever, and lichenification of the skin in young persons with a constitutional predisposition to hypersensitivity. The author points out that this syndrome should include cataract formation as an uncommon addition. Ten cases are reported in detail. On two occasions intradermal tests with aspirated aqueous gave negative reactions. Histologic examination of the crystalline lens in two instances showed cortical degeneration and normal capsule. The roles of infection, avitaminosis, endocrine deficiency, and a disturbance of the autonomic nervous system as the causative factors in producing these cataracts are briefly discussed, but seem less attractive than an allergic (atopy) basis.

J. Hewitt Judd.

Benoit, Maurice. **Arachnodactyly with dislocated lenses.** Bull. Soc. d'Opht. de Paris, 1938, May, p. 182.

Benoit reports a case of Marfan's syndrome in a 15-year-old boy. In addition there was anisocoria and divergent strabismus. George A. Filmer.

Bolettieri, Daniele. **A peculiar malformation of the anterior segment of the eye characterized by congenital cataract and pigmented digitations.** Boll. d'Ocul., 1939, v. 18, Sept., pp. 729-742.

A boy of 12 years and a man of 22 years each showed congenital cataract of one eye. Adherent to the cataract were numerous finger-like formations of the same color as the iris and running from the nasal side of the ciliary body toward the center of the cataract. The writer is of the opinion that these formations were the result of an intrauterine cyclitic process. (Bibliography, 3 figures.) M. Lombardo.

Chitnis, V. K. **Evolution of cataract operation in the Sir C. J. Ophthalmic Hospital, Bombay.** Proc. All-India Ophth. Soc., 1938, v. 6, pp. 98-105.

Chitnis presents a historical consideration of the cataract operation in India, where it was performed many hundreds of years before it was attempted in the West. Even today enormous numbers of couching operations are done. The various operators and their particular methods in the Sir C. J. Ophthalmic Hospital since 1823 are thoroughly reviewed, and the statements of percentages presented would make fine material for a present-day paper on "various cataract operations."

Lawrence G. Dunlap.

Dutt, K. C. **Posture treatment of the iris in lever action intracapsular extrac-**

tion of cataract. Arch. of Ophth., 1940, v. 23, May, pp. 908-917.

To prevent prolapse of the intact iris, the author urges the combination of three procedures: (1) posture treatment by raising the head of the bed 9 inches, (2) toning up of the iris muscles by the use of physostigmine salicylate, and (3) the use of three small conjunctival flaps to guard the three strategic vulnerable points at the three, nine, and twelve o'clock positions. The article includes a review of the various methods advocated in the literature.

J. Hewitt Judd.

Ecker, E. E., and Pillemer, L. **The specificity of oxidized and reduced proteins of the ocular lens.** Jour. Exper. Med., 1940, v. 71, May 1, p. 585.

As a continuance of studies revealing that species specificity of the keratins is dependent on the oxidation-reduction state of the sulphohydryl groupings in the protein, lens protein which is rich in sulphohydryl sulphur was studied in the ocular lenses of fish, sheep, swine, and chickens. Species specificity was demonstrable in protein from chicken and fish lenses, but was not so evident in the protein from swine and sheep. Serologic differences could be detected in the lens protein of a single species, depending on the redox state of the protein.

Edna M. Reynolds.

Fischer, F. P. **The yellow-brown pigments of the lens.** Ophthalmologica, 1940, v. 99, May, p. 425.

The yellow to brown substances that develop in the aging lens are melanoidines. These are condensation compounds of amino acids or amines with carbohydrates and are not humines or malanin. They protect the eye and lens from the toxic action of the catabolic production of protein disintegration. It is the amines, particularly, that are a cause of edogenous endophthalmitis. These amines occur in the cortex, but not in a nucleus which has become yellow. F. Herbert Haessler.

Flieringa, H. J. **A practical tip for intracapsular extraction.** Ophthalmologica, 1940, v. 99, May, p. 434.

The author injects a minimal amount of epinephrine subconjunctivally at the limbus to prevent contraction of the pupil and to facilitate grasping the lens capsule. F. Herbert Haessler.

François, Jules. **An experimental study of the influence of immunologic factors upon the production of cataract.** Bull. Soc. Belge d'Opht., 1940, no. 79, p. 110.

In a former study the author claims to have demonstrated that the lens proteins possess antigenic properties and that their injection into a test animal gives rise to specific protein in the blood serum. He deduces from this fact that these precipitins may be diffused throughout the lens and upon solution within the transparent lens albumins produce an opaque precipitate or cataract. By experiments upon rabbits the author has tried to prove that the above is not a simple hypothesis but a real fact. He concludes as follows: The injection of 24 pregnant rabbits with a lens emulsion caused congenital lens opacities in the offspring. The lenses of the injected does were unaffected. The same was true of 86 adult rabbits injected in an earlier experiment. The lens of the adult rabbit seems to be impermeable to the precipitins, but this is not true of the lens of the fetus, and congenital cataract may be explained

as an immunologic phenomenon. (12 figures, 2 references.)
Jerome B. Thomas.

Garrow, A., and Michaelson. I. C. **A case of exfoliation of the lens capsule with the pathological report.** Brit. Jour. Ophth., 1940, v. 24, Aug., pp. 400-403.

A man aged 69 years, apparently in robust health, complained of defective vision of a year's duration. He was found to have a detachment of the right retina with an intraocular tumor. The other eye showed exfoliation of the lens capsule but no signs of glaucoma. The cataract in this eye was later extracted, recovery being usual. (Figures, references.) D. F. Harbridge.

Gradle, H. S., and Sugar, H. S. **Concerning the chamber angle. 2. Exfoliation of the zonular lamella and glaucoma capsulare.** Amer. Jour. Ophth., 1940, v. 23, Sept., pp. 982-997.

Harris, C. F. **Bilateral anterior lenticonus.** Northwest Med., 1940, v. 39, June, pp. 219-220.

The author reports a case of true bilateral anterior lenticonus, complicated by bilateral, discoid, punctate cataracts. In each lens was a round, finely granular opacity just behind the nucleus, with the anterior capsule and cortex globular in form protruding through the pupil to within approximately 0.5 mm. of the posterior surface of the cornea. T. E. Sanders.

Kirwan, E. O'G. **A new intracapsular extraction forceps.** Proc. All-India Ophth. Soc., 1938, v. 6, p. 199.

For the past six years Kirwan has done the intracapsular cataract extraction as the operation of choice. He has developed a forceps which is a modification of the Elschnig forceps but with a broader grip to make manipulation easier. Lawrence G. Dunlap.

Marx, E. **Lens changes in young diabetic patients.** Ophthalmologica, 1940, v. 99, May, p. 286.

The author describes lens changes observed biomicroscopically in three young diabetics. The first patient had the characteristic subcapsular opacities (first described by Schneider) plus a sharply defined opacity in the center of the fetal nucleus. The normally clear area just beneath the capsule was clouded in several places. In the second patient the opacities characteristically seen in the subcapsular region of the cortex were found throughout the entire lens with the exception of a vertical clear central interval in the fetal nucleus. The posterior cortex contained a thin flat opacity in the zone immediately under the capsule. The third patient became myopic rather suddenly, and at the same time peculiar opacities appeared in the lens, the most striking of which were vacuoles in the deeper parts of the anterior cortex, but which soon involved the entire anterior cortex. F. Herbert Haessler.

Mikhailov, A. X. **Scissors for cataract extraction.** Viestnik Opht., 1940, v. 16, pt. 4, p. 254.

The author has designed a pair of scissors sharp on the outside edges, and cutting out as they are opened. The limbus is punctured and the incision enlarged by opening the scissors. It is claimed that this type of section does not become complicated by the iris falling over the knife. (Illustrations.) Ray K. Daily.

Mulock Houwer, A. W. **Bilateral operation for senile cataract.** Ophthalmologica, 1940, v. 99, May, p. 269.

Because of economic conditions, it became necessary to be sparing with hospital bed-days. The author decided, with some mental reservation, to operate on both eyes of patients with senile cataract at the same time. The advantages are that it is less expensive and gives less discomfort to the patient. In 99 out of 117 patients he had good results in both eyes. Fifteen had a good result in at least one eye. In four patients one eye was lost. A diabetic lost both eyes, and one patient died soon after operation. There was no tendency for mishaps to occur in both eyes. Infection did not become bilateral. There is only a slight chance that both eyes will be lost, and against this one can balance the disadvantage to the patient resulting from the loss of courage on the part of doctor or patient to operate on the second eye when the first has been lost. In cases of poor surgical risk, only one eye is operated upon at a time. F. Herbert Haessler.

Spaeth, E. B. **The management of some complications which follow cataract extraction.** Amer. Jour. Ophth., 1940, v. 23, Sept., pp. 1019-1028.

Spratt, C. N. **A streamlined cataract knife.** Amer. Jour. Ophth., 1940, v. 23, Sept., pp. 1040-1041.

Weekers, Roger. **Glycolysis of the lens.** Bull. Soc. Belge d'Opht., 1940, no. 79, p. 44.

The existence of three systems of oxyreduction in the lens has been demonstrated: ascorbic acid, glutathione, and lactoflavine. Apparently the lens metabolism depends upon the contribution of these substances by the aqueous humor, but their exact rôle is not known. The maintenance of a normal energy balance requires the contribution of nutritive substances, the elimination of waste products, and the presence of catalysts. The least alteration in this delicate ensemble may lead to a change in the optical qualities of the lens. (15 references.)

Jerome B. Thomas.

10

RETINA AND VITREOUS

Agatston, S. A. **Clinicopathologic study of diabetic retinitis.** Arch. of Ophth., 1940, v. 24, Aug., pp. 252-257.

This is a preliminary report of work still in progress. It is pointed out that while the presence of hyperglycemia may be responsible for metabolic changes in arterial walls, the effect is even more specific on capillaries and veins. Since the tendency to hemorrhage is the basis of diabetic retinitis and all other changes are secondary, one does not have to go beyond the venocapillary system for a solution of pathogenesis. In studying the venules of 25 retinas, fibrosis of the intima was found in nine, in eight others the media showed separation of longitudinally directed collagen fibrils, and in two retinas there was a thickening of the media due to the deposit of collagen. Diseased retinal capillary loops and networks stood out because of their rigid patency, dilated lumens, and thickened walls. These changes are shown in photomicrographs. J. Hewitt Judd.

Aliquó-Mazzei, Allessandro. **Traumatic ruptures of the retina without detachment, healed spontaneously.** Boll. d'Ocul., 1939, v. 17, April, pp. 263-269. (See Section 16, Injuries.)

Banaji, B. P. **Opacities of the vitreous humor in the middle-aged.** Proc. All-India Ophth. Soc., 1938, v. 6, pp. 127-129.

The author gives a very clear discussion of the sudden appearance of vitreous opacities in middle-aged persons in whom the lesion has nothing to do with constitutional disorders or focal infection. He attempts to reassure his patients as to the harmlessness of the symptoms and advises them to rest from near work for a week or so and avoid glare. Lawrence G. Dunlap.

Basile, Giambattista. **A peculiar constitutional predisposition to thrombosis of the central retinal vein.** Boll. d'Ocul., 1939, v. 18, Sept., pp. 743-763.

Studies were made on the blood of 11 patients, seven of whom were affected by thrombosis of the central vein and four by hemorrhagic glaucoma secondary to a thrombosis. The age of the patients ranged from 34 to 75 years. Tabulated results show that these patients had constitutional disturbances of the neurovegetative system consisting of an exaggeration of the oculocardiac reflex of Dagnini-Ascher, a tendency to blood-vessel spasm, intestinal spasm, hyperchlorhydria, marked dermographism, bradycardia, and respiratory arhythmia. The blood serum showed low globulin content, slow coagulation time, and slow sedimentation rate. The writer concludes that thrombosis of the central vein is related to a constitutional predisposition due to increased vagus tonicity. (Bibliography.) M. Lombardo.

Binkhorst, P. G. **Statistical observations on retinal detachment.** Ophthalmologica, 1940, v. 99, May, p. 367.

Of 515 eyes with retinal detachment operated upon by Weve, 394 (77 percent) were permanently cured. For statistical purposes, the retinal detachments are divided into eight groups. The percentage of cures in these groups varies from 22 to one hundred. In 53 there were complications, namely, hemorrhage in 25, noninfectious inflammatory reactions in 12, and acute postoperative hypotony in 16. In 41 cases there was recurrence, and that ten times more frequently from a new tear than from inadequate sealing of the first rupture.

F. Herbert Haessler.

Biswas, P. K. **Recurrent hemorrhages in young adults—Eales's disease—with reports of two cases.** Proc. All-India Ophth. Soc., 1938, v. 6, pp. 134-139.

The author discusses Eales's disease as a hemorrhage not associated with exertion or trauma nor related to hemorrhages elsewhere in the body. The macula and fovea always escape and the vision, although first greatly impaired, may return rapidly to normal. Tuberculin is stressed as being the best treatment. Secondary glaucoma is often present but ordinarily the prognosis is good. Lawrence G. Dunlap.

Hurst, J. H. **Actinomycosis progressively involving retina, lungs, and vertebrae.** Med. Bull. Veterans' Admin., 1940, v. 17, July, p. 90.

Hurst reports the fatal case of a soldier who apparently had had widespread actinomycosis for several years. The lesion in the eye had been diagnosed as tuberculous. The mode of entry of the actinomycosis was uncertain although it was suggested that possibly it had been through an injury in a football game. Ralph W. Danielson.

Huysmans, J. **Exudative central detachment of the retina in a family (macular pseudocysts).** Ophthalmologica, 1940, v. 99, May, p. 449.

The author describes a family of 11

members of whom eight were affected with a peculiar macular lesion which could be adequately analyzed only with the binocular ophthalmoscope. The lesion, which had a sharp contour, was a definitely raised globule in the foveal area. By red-free light no disturbance of the normal yellow was seen. Photographs illustrate the condition. Strikingly, no alteration in function was associated with these macular cysts.

F. Herbert Haessler.

Kornzweig, A. L. **Anomalous retinal vein crossing the macula.** Arch. of Ophth., 1940, v. 24, Aug., pp. 362-366.

A case of an anomalous retinal vein in the fundus of a girl of 19 years is presented. This vein, a tributary of the inferior temporal vein, passed directly across the macular region and dipped slightly below the fovea. The vessel was plotted by angioscotometry up to and beyond the fovea. An attempt to explain this anomaly is made. (Fundus photographs.) J. Hewitt Judd.

Laughlin, C., Thomas, C. B., and Friedenwald, J. S. **The retinal arteries in experimental renal hypertension: significance of localized caliber constriction.** Bull. Johns Hopkins Hosp., 1940, v. 67, Aug., p. 79.

The authors produced experimental hypertension in a dog by Goldblatt's method of partially occluding the renal arteries. They then made drawings and photographs of the retina. The eye was afterward enucleated and cut in serial sections and, by special technique, the localized histologic changes in the retinal arteries were correlated with the ophthalmoscopic findings. By this method it was shown that localized arterial constrictions seen ophthalmoscopically may occur either with or without corresponding histologic changes, and likewise histologic changes may be present either with or without a corresponding clinical constriction. It is noteworthy that in dogs with experimental renal hypertension, persistent localized constrictions may be seen ophthalmoscopically in arteries in which no organic changes are demonstrable in the vessel wall at the constricted points. It is concluded that such constrictions are due to arterial spasm. (6 references.)

Ralph W. Danielson.

McAlester, A. W., 3rd. **A simple method of localizing large retinal tears.** Amer. Jour. Ophth., 1940, v. 23, Oct., p. 1161.

Mistretta, R. **Occlusion of the central retinal artery not affecting the macular zone.** Boll. d'Ocul., 1939, v. 18, Oct., pp. 825-830.

A man of forty years who a few days before had noticed sudden diminution of vision in the right eye showed a milky-white discoloration of the entire retina with the exception of a small tract corresponding to the papillomacular region which appeared to be normal. At the temporal side of the disc an artery emerged taking a course toward the macular region where it ended forming numerous branches. The vision was 3/10. Acetylcholine was used and the vision improved to 10/10 following the first injection. The writer believes that this was a case of retinal angiospasm and the preservation of central vision during the first period of the spasm was related to the presence of the unusual course of the cilioretinal artery. (Bibliography, 3 figures.)

M. Lombardo.

Puntenney, Irving. **The effect of certain physical and chemical stimuli on**

the caliber of the retinal blood vessels in man. Amer. Jour. Ophth., 1940, v. 23, Oct., pp. 1113-1122.

Rooy, A. J. P. M. de. **The relationship between venous pressure of the retina and intracranial pressure.** Ophthalmologica, 1940, v. 99, May, p. 484.

Opinions differ on this topic. The author presents his measurements on patients and on dogs whose intracranial pressure had been raised artificially. He found a definite correspondence between the two values.

F. Herbert Haessler.

Van Waveren, W. F. J. **Amotio retinae attending scleritis and its possible relations with Harada's disease.** Ophthalmologica, 1940, v. 99, May, p. 543.

In a woman of 41 years with recurring attacks of scleritis, retinal detachment occurred in one eye and papilledema in the other. With surgical treatment, the retina became adherent throughout. The author was able to find only a few communications about retinal detachment as a complication of scleritis. F. Herbert Haessler.

Weve, H. M., and Fischer, F. P. **The origin and composition of the subretinal fluid in ruptural retinal detachments.** Ophthalmologica, 1940, v. 99, May, p. 291.

Analysis of the subretinal fluids of forty eyes with retinal detachment showed that in new cases the fluid was identical with that obtained from the vitreous after hysteresis. If the detachment persists, this fluid becomes mixed with heavy water which is normally found only in the pigment epithelium of the retina. Changes in the permeability of this layer allow the heavy water to escape and then protein also passes into the fluid. The speed of this exchange of substances depends on the state of the pigment epithelium and choroidal vessels, and this decides the fate of the detached retina.

F. Herbert Haessler.

NEWS ITEMS

Edited by Dr. H. Rommell Hildreth
640 South Kingshighway, Saint Louis

News items should reach the Editor by the twelfth of the month

Miscellaneous

Expansion and speed-up production, made necessary by national-defense plans, increase the hazards which result in eye injuries and other types of accidents, it is pointed out by Mrs. Eleanor Brown Merrill, executive director of the National Society for the Prevention of Blindness, in announcing the appointment of an industrial advisory committee, headed by Dr. Leonard Greenburg, executive director of the Division of Industrial Hygiene, New York State Department of Labor.

"Industrial eye diseases and eye accidents constitute one of the principal causes of blindness in America. Although industry has made much progress in the campaign to protect the sight of workmen, new processes have created additional hazards. The national-defense program, necessitating the employment of large numbers of men in new jobs—working in strange surroundings, perhaps in plants operating on a 24-hour basis—makes for an inevitable increase in the danger of accidents. Some of these new employees are untrained, or use operations that are unfamiliar.

"To deal with these problems and other matters concerning the protection of workmen from eye diseases and eye accidents, the National Society for the Prevention of Blindness decided to appoint an industrial advisory committee of outstanding authorities. The society also has under way an exhaustive study of the entire problem of eye hazards in industry, and will make this public shortly."

The fifth semi-annual post-graduate course in Neuro-Muscular Anomalies of the Eyes was given by Dr. George P. Guibor at Children's Memorial Hospital, Chicago, Illinois, from November 10-15, 1940.

The subject for the Treacher Collins Prize Essay is announced as being: "Allergic affections of the eye and its adnexa." The essays must be written in English and submitted to the Honorable Secretary, Ophthalmological Society of the United Kingdom, 5, Racquet Court, Fleet Street, E. C. 4, on or before December 31, 1941.

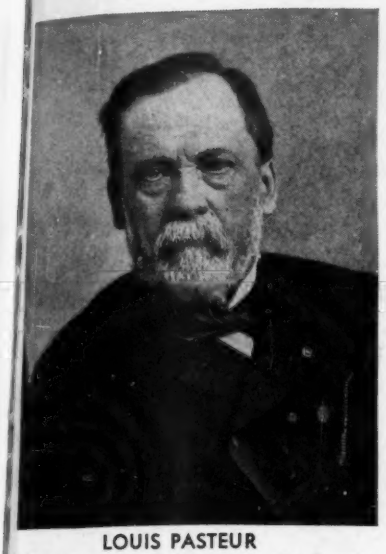
Personals

Dr. M. Pinson Neal of Columbia, Missouri, professor of pathology, University of Missouri School of Medicine, was awarded the Mississippi Valley Medical Society's Distinguished Service Award for 1940 at the annual banquet of the society held at Rock Island, Illinois, September 26th. The award is given annually to an active member of the society for "unusual and distinguished service to the medical profession."

Word has been received of the retirement of Dr. John Herbert Waite as acting head of the Department of Ophthalmology of Harvard University, and of the appointment of Dr. Edwin B. Dunphy as Williams Professor of Ophthalmology of that Institution.

Dr. D. G. Cogan has been appointed head of Howe Ophthalmic Laboratory, to succeed Dr. Frederick H. Verhoeff.

Before Pasteurization was first Introduced in 1863...



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SEASON'S GREETINGS

At this Holiday Season we extend our Cordial Thanks and Appreciation for the Many Evidences of your Friendship during the Past Year.

May we Express a Sincere Wish that the New Year will bring to You and Yours Health and Security.

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